

**Demystifying Medicine 2018**

# **Emerging Infections: A Perpetual Challenge**

**Anthony S. Fauci, M.D.**

**Director**

**National Institute of Allergy and  
Infectious Diseases**

**National Institutes of Health**

**January 9, 2018**



**THE  
HILL**

January 13, 2017

**White House Holds  
Disaster-Response  
Exercise with  
Trump Officials**



# The NIH Record

U.S. Department  
of Health  
and  
Human Services

November 20  
1984  
Vol. XXXVI  
No. 24

National  
Institutes  
of  
Health

## Dr. Anthony Fauci, Expert on Immunity and AIDS, Named Director of Nat'l. Institute of Allergy and Infectious Diseases

Dr. Anthony S. Fauci has been named Director of the National Institute of Allergy and Infectious Diseases, effective Nov. 2.

NIAID conducts and supports research to better understand the causes of allergic, immunologic and infectious diseases, and to develop better means of preventing, diagnosing and treating such illnesses.

Dr. Fauci, 43, an internationally renowned expert on the immune system, has been chief of NIAID's Laboratory of Immunoregulation since 1980 and deputy clinical director of the Institute since 1977.

"I am extremely pleased that Dr. Fauci will take over the leadership of this important institute," HHS Secretary Margaret M. Heckler said in announcing the appointment. "His unique background, particularly in the fields of immunology and infectious diseases, will be of key importance in maintaining and accelerating our momentum in these crucial



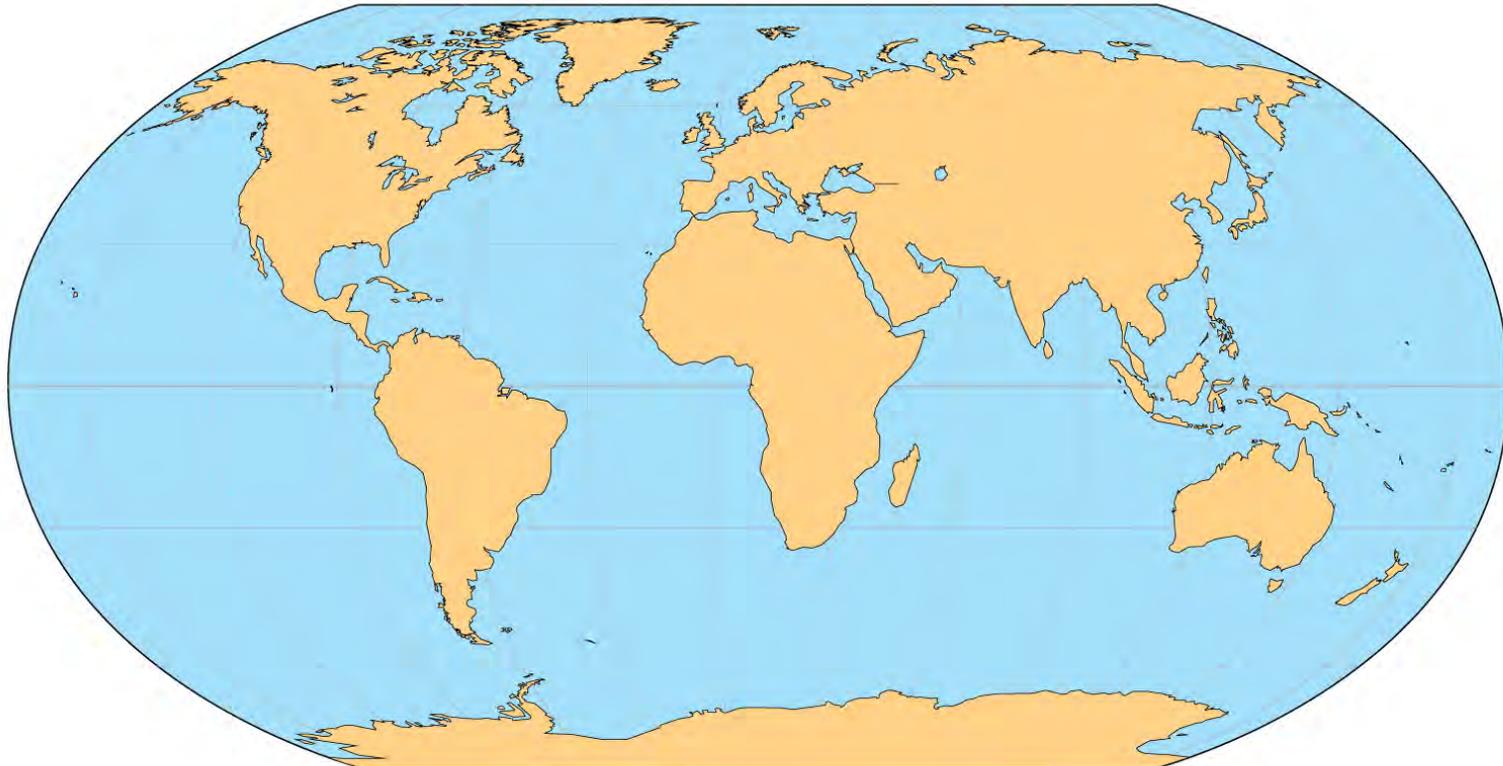
**Dr. Fauci is internationally renowned for his expertise on the immune system.**

# Testimony before the House Appropriations Subcommittee for NIH – 1980s



# Global Examples of Emerging and Re-Emerging Infectious Diseases

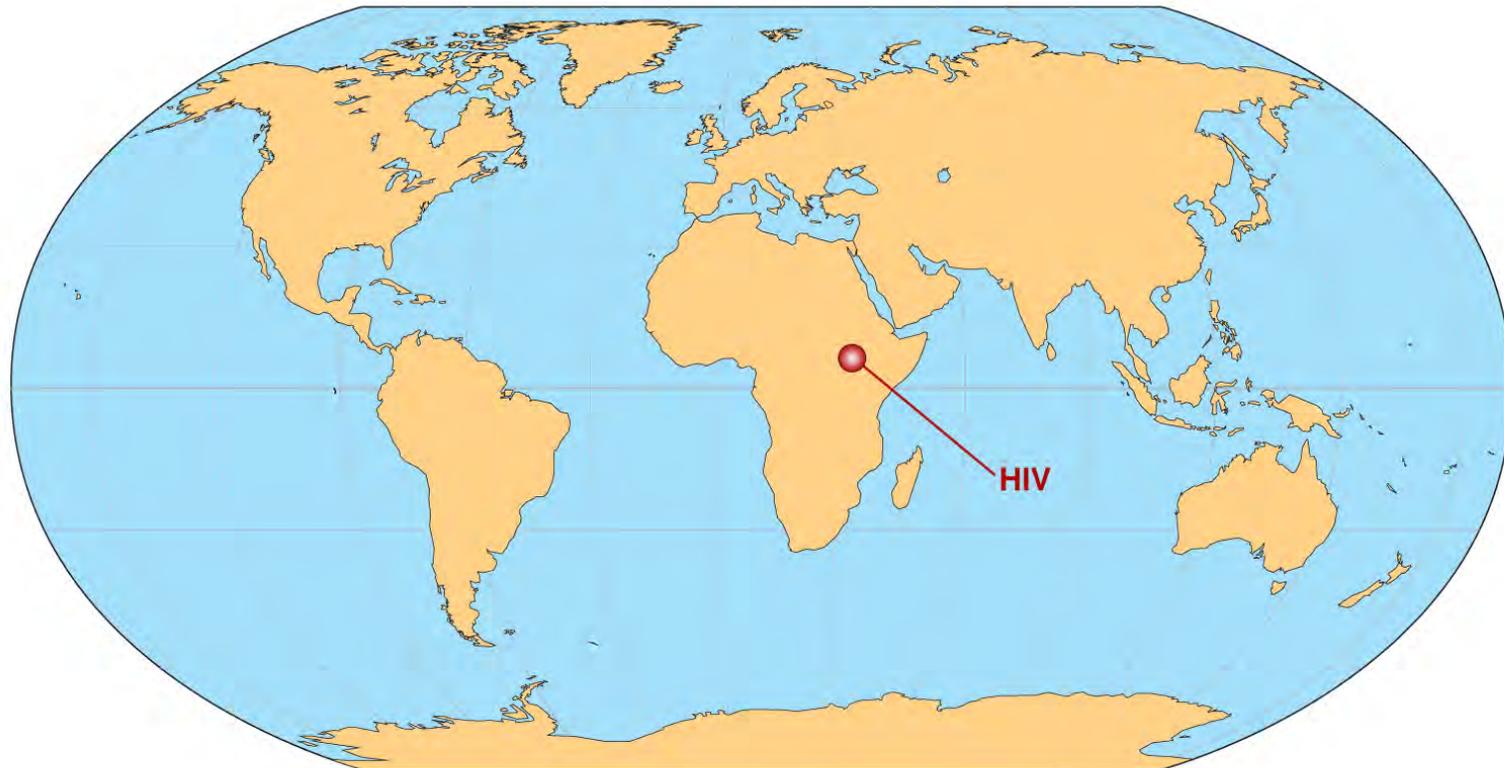
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● Newly emerging    ● Re-emerging/resurging    ● “Deliberately emerging”

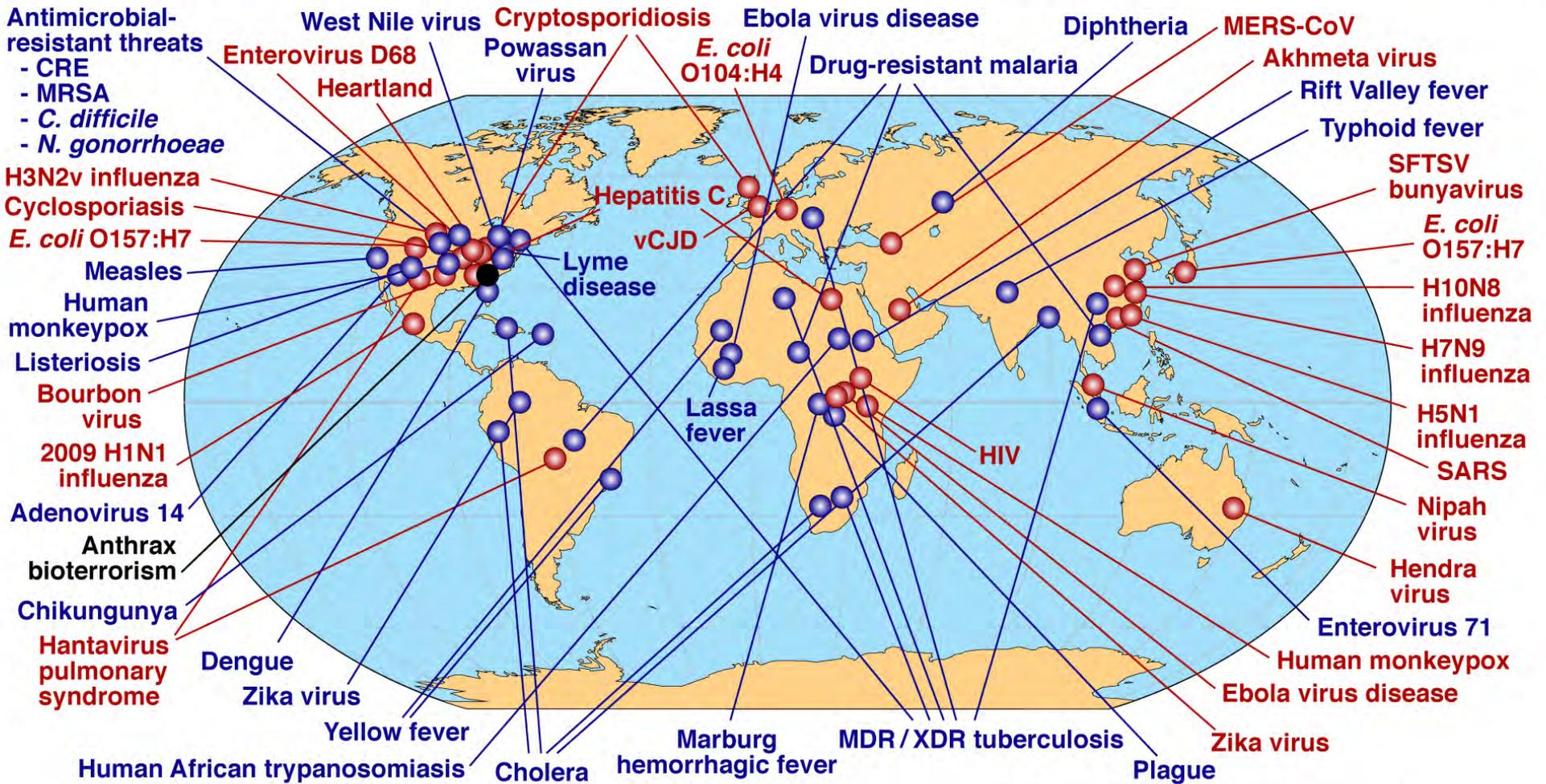
# Global Examples of Emerging and Re-Emerging Infectious Diseases

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● Newly emerging    ● Re-emerging/resurging    ● “Deliberately emerging”

# Global Examples of Emerging and Re-Emerging Infectious Diseases



● Newly emerging    
 ● Re-emerging/resurging    
 ● “Deliberately emerging”

# Five Administrations and Emerging Infectious Diseases

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**Ronald W. Reagan 1981-1989**



**George H.W. Bush 1989-1993**



**William J. Clinton 1993-2001**



**George W. Bush 2001-2009**



**Barack H. Obama 2009-2017**





■ HIV/AIDS

**Ronald W. Reagan**  
**1981-1989**

CENTERS FOR DISEASE CONTROL

**MNWR**<sup>TM</sup>

MORBIDITY AND MORTALITY WEEKLY REPORT

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June 5, 1981

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***Pneumocystis Pneumonia -  
Los Angeles***

July 3, 1981

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***Kaposi's Sarcoma and  
Pneumocystis Pneumonia  
Among Homosexual Men -  
New York City and California***

1 June 1982

Volume 96

Number 6

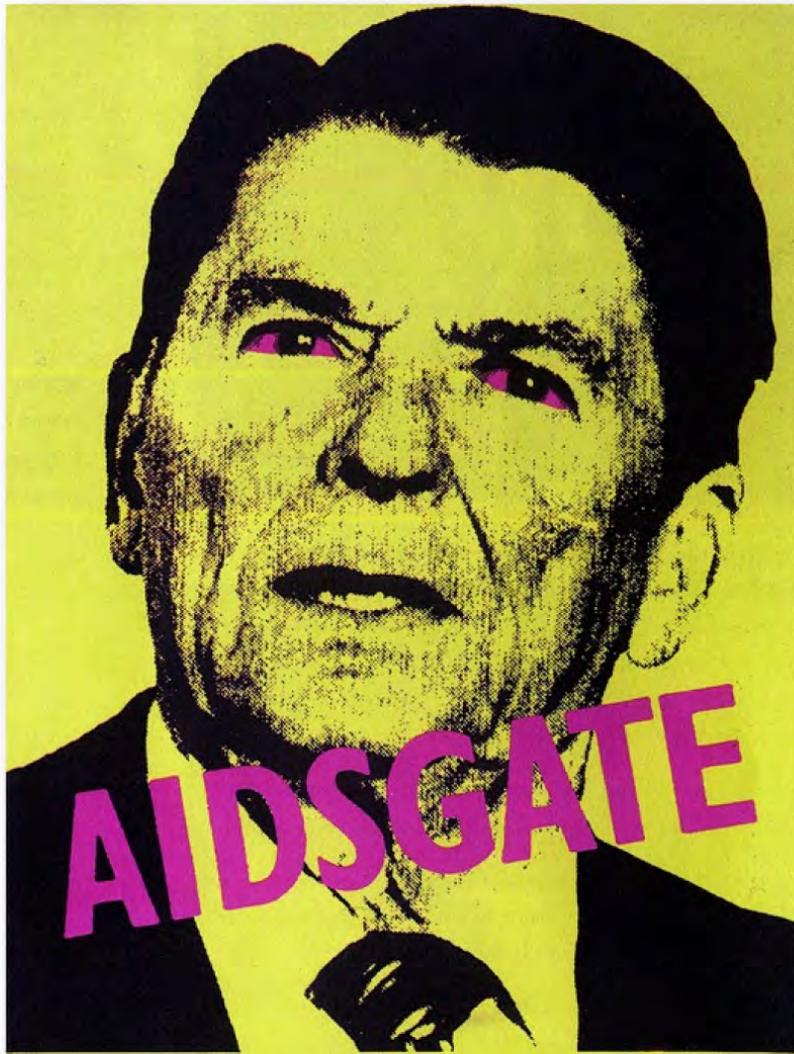
# Annals of Internal Medicine

Published Twice Monthly by the American College of Physicians

## **The Syndrome of Kaposi's Sarcoma and Opportunistic Infections: An Epidemiologically Restricted Disorder of Immunoregulation**

Anthony S. Fauci, M.D.

*"...because we do not know the cause of this syndrome, any assumption that the syndrome will remain restricted to a particular segment of our society is truly an assumption without scientific basis."*



**This Political Scandal Must Be Investigated!**

54% of people with AIDS in NYC are Black or Hispanic... AIDS is the No. 1 killer of women between the ages of 24 and 29 in NYC...

By 1991, more people will have died of AIDS than in the entire Vietnam War... What is Reagan's real policy on AIDS?

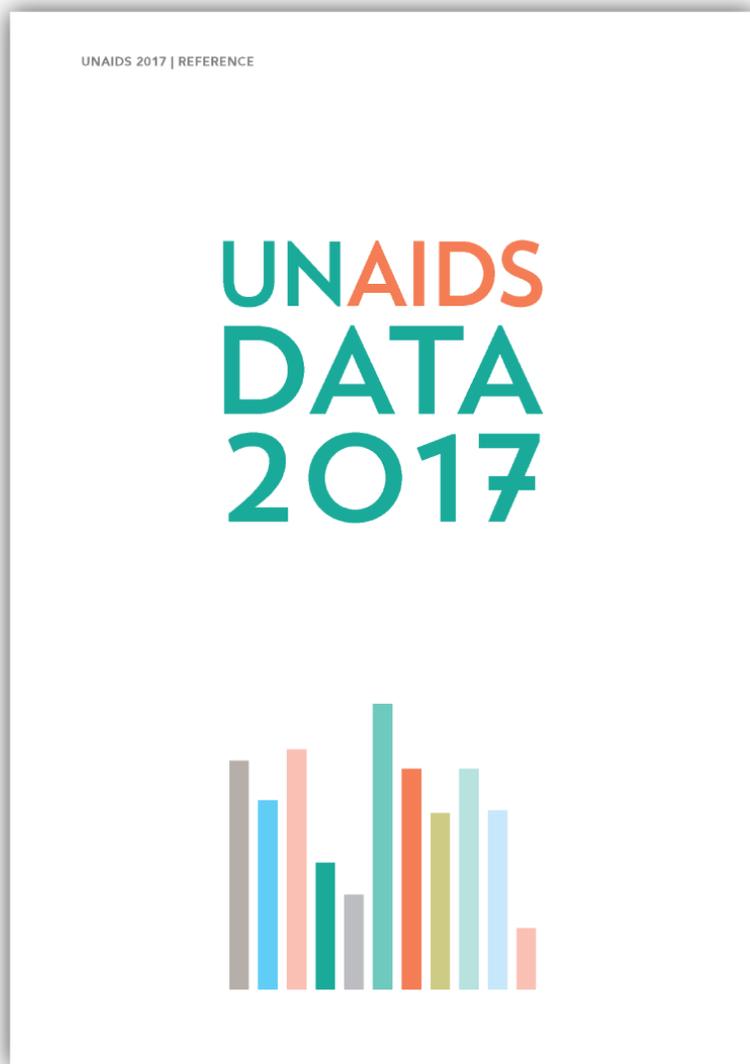
Genocide of all Non-whites, Non-males, and Non-heterosexuals?...

SILENCE = DEATH



# UNAIDS Global AIDS Update, 2017

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- **In 2016:**
  - 36.7 million living with HIV
  - 1.8 million infected with HIV
  - 1.0 million deaths from AIDS-related illnesses
- **Since start of the pandemic**
  - 76.1 million infected with HIV
  - 35.0 million deaths from AIDS-related illnesses



■ HIV/AIDS

**George H. W. Bush**  
**1989-1993**

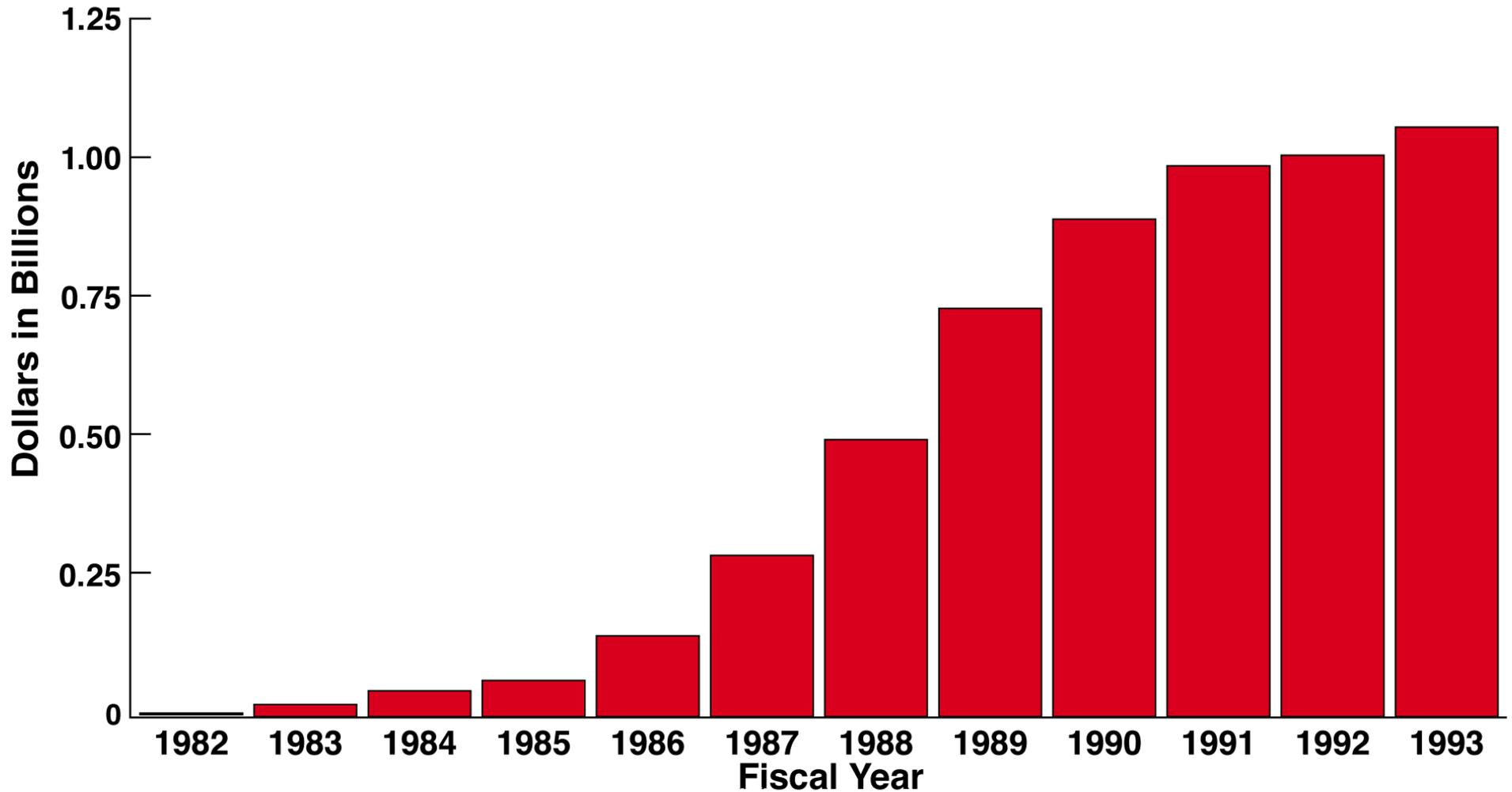


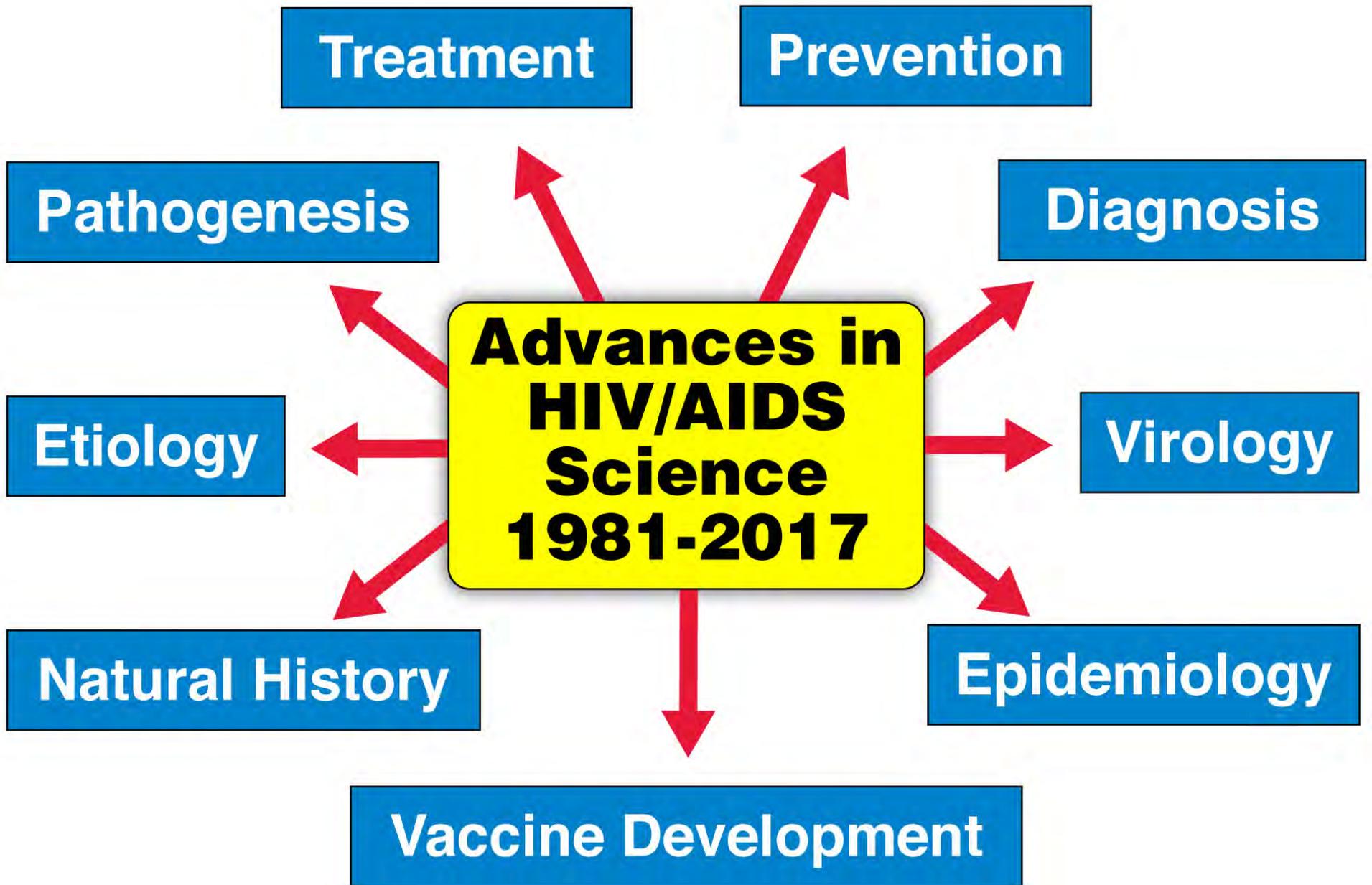


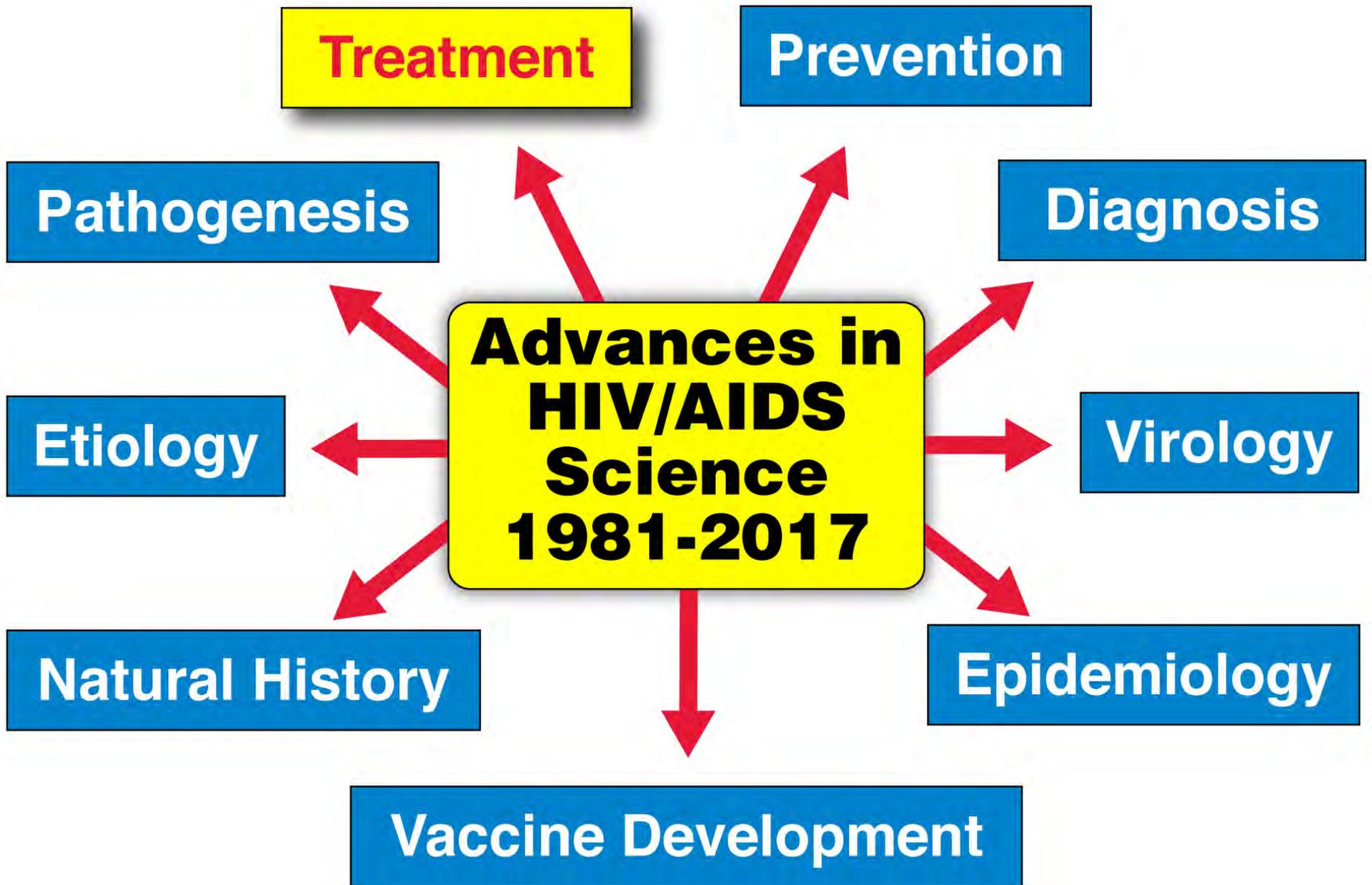


# NIH HIV/AIDS Research Funding, FY 1982 to FY 1993

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# **Rounds at NIH Clinical Center, Early 1980s – AIDS Patient**

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■ Median survival of AIDS patients: ~8-15 months

# FDA-Approved Antiretroviral Drugs

## NRTI

- 5 multi-drug combinations
- Abacavir
- Didanosine
- Emtricitabine
- Lamivudine
- Stavudine
- Tenofovir (TDF, TAF)
- Zidovudine

## NNRTI

- Delavirdine
- Efavirenz
- Etravirine
- Nevirapine
- Rilpivirine

## Integrase Inhibitors

- Dolutegravir
- Elvitegravir
- Raltegravir



## PI

- Atazanavir
- Darunavir
- Fosamprenavir
- Indinavir
- Lopinavir/Ritonavir
- Nelfinavir
- Ritonavir
- Saquinavir
- Tipranavir

## Entry Inhibitor

- Maraviroc

## Pharmacokinetic Enhancers

- Cobicistat
- Ritonavir

## Multi-Class Combinations

- Atripla
- Complera
- Genvoya
- Odefsey
- Stribild
- Triumeq
- Juluca

## Fusion Inhibitor

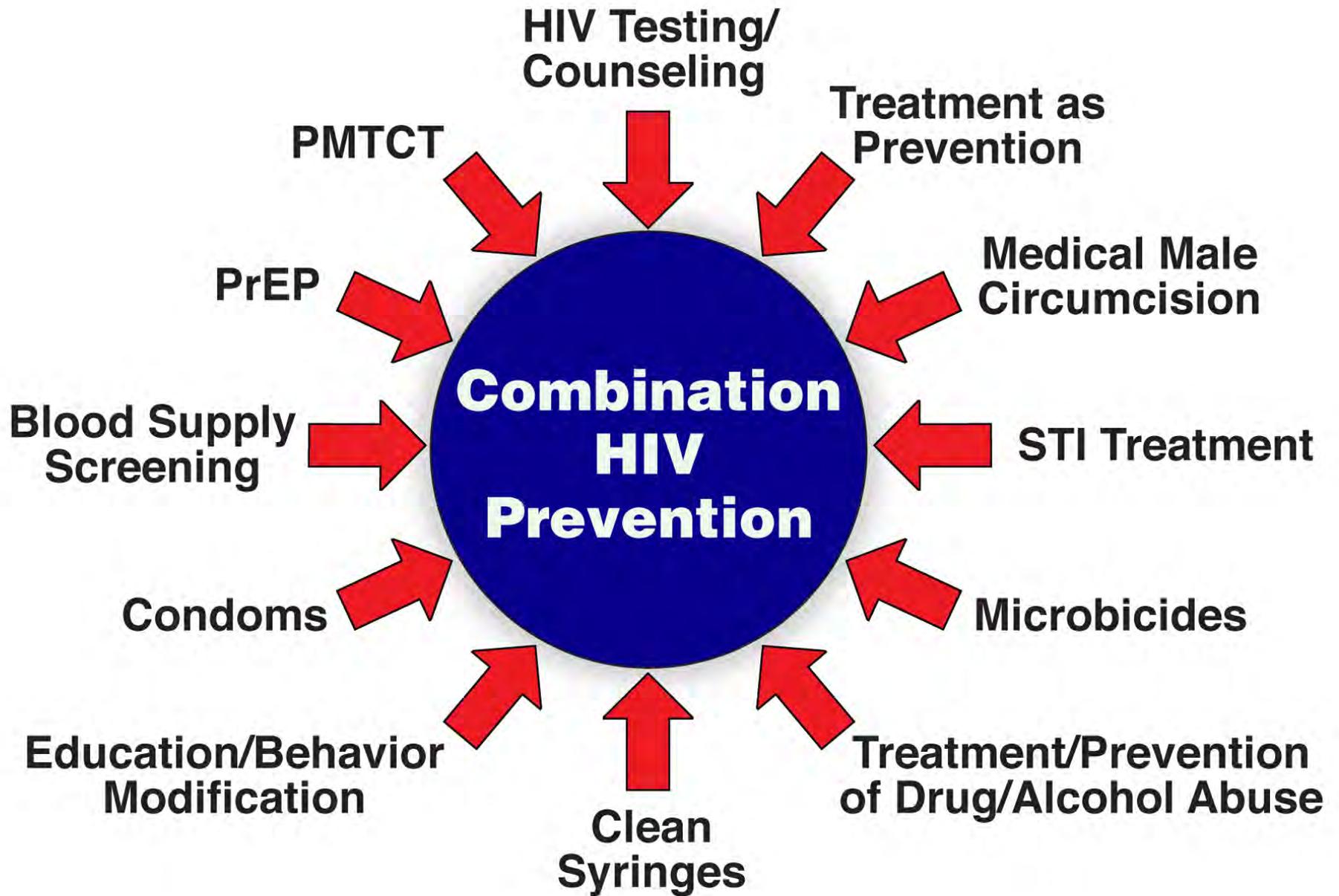
- Enfuvirtide

# **Life Expectancy for 20-Year-Old Newly Diagnosed with HIV, 1980s and Today**

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**1980s  
(no ART)** | **1-2 years from  
AIDS diagnosis**

**Today  
(on ART)** | **~53  
years**

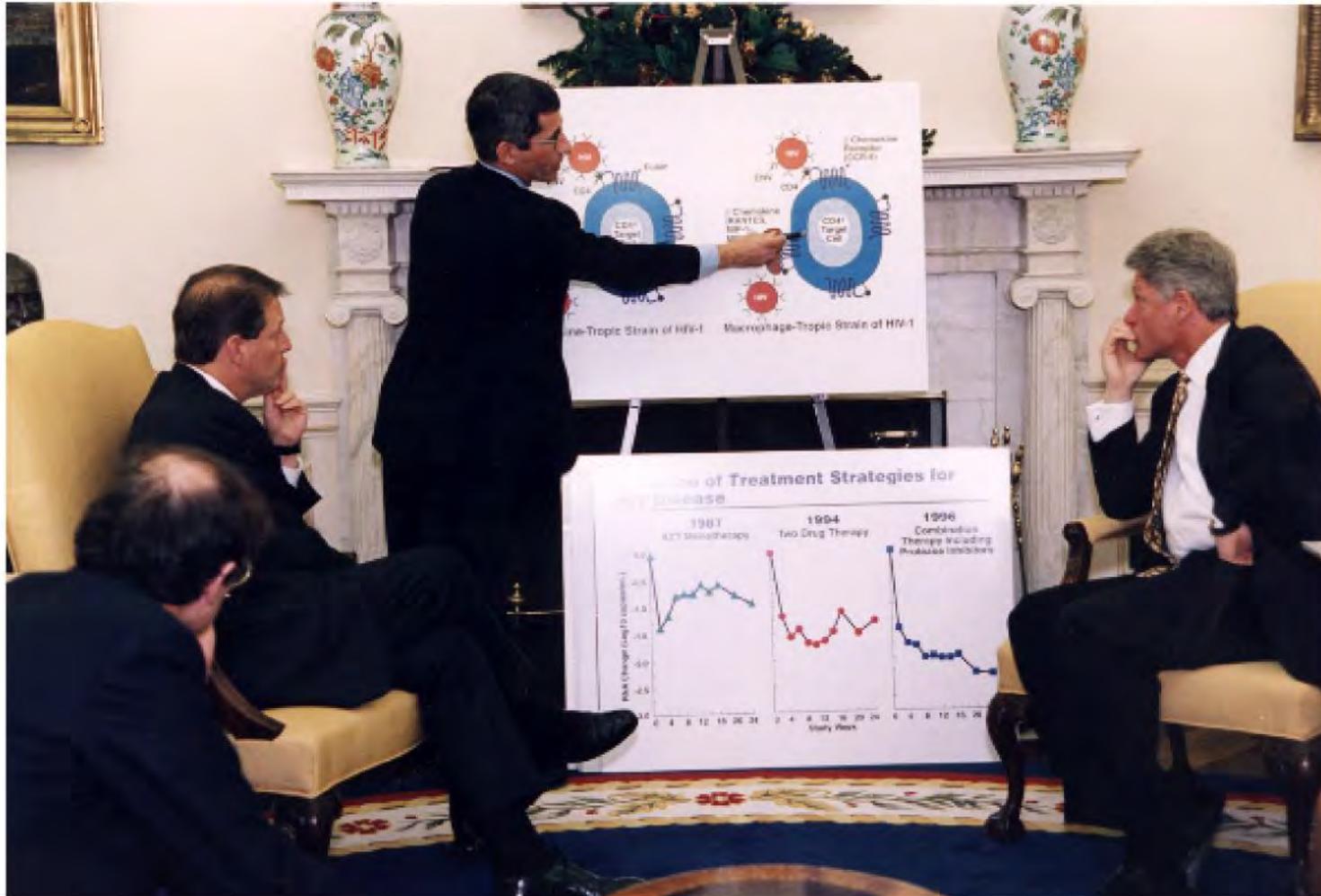




**William J. Clinton**  
**1993-2001**

- **HIV/AIDS**
- **West Nile Virus**
- **H5N1 Influenza**
- **Antimicrobial Resistance**

# Meeting at the White House to Discuss AIDS Research, Dec. 3, 1996



# **Commencement Address by President Clinton at Morgan State University, Baltimore, May 18, 1997**

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**"If America commits to find an AIDS vaccine and we enlist others in our cause, we will do it... Today I'm pleased to announce the National Institutes of Health will establish a new AIDS vaccine research center dedicated to this crusade."**



# VRC Research: From HIV to Zika

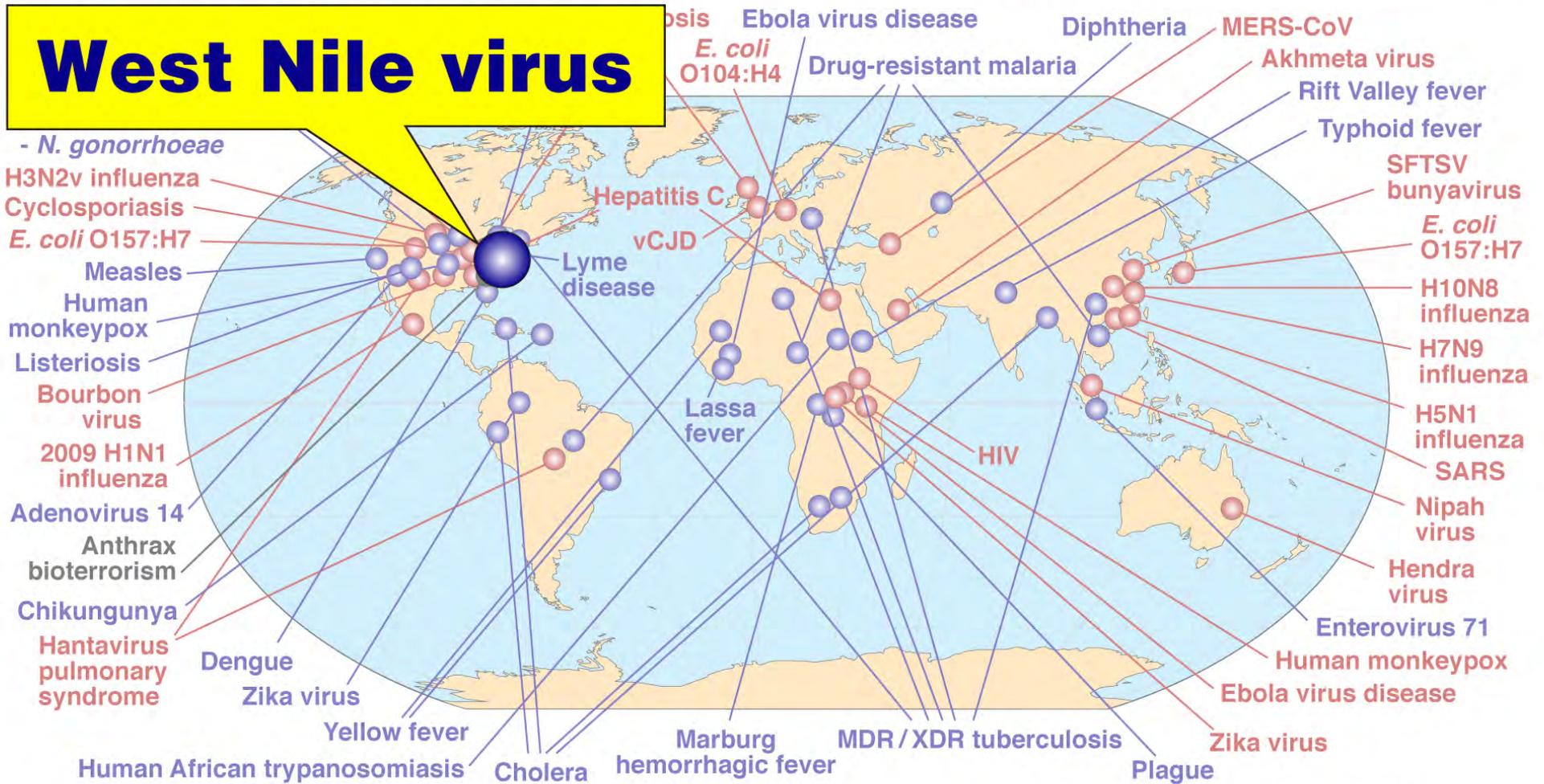
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- HIV
- West Nile virus
- Chikungunya
- Ebola/Marburg
- Influenza
- Malaria
- MERS-CoV
- RSV
- Tuberculosis
- Venezuelan, Eastern, and Western equine encephalitis viruses
- Zika

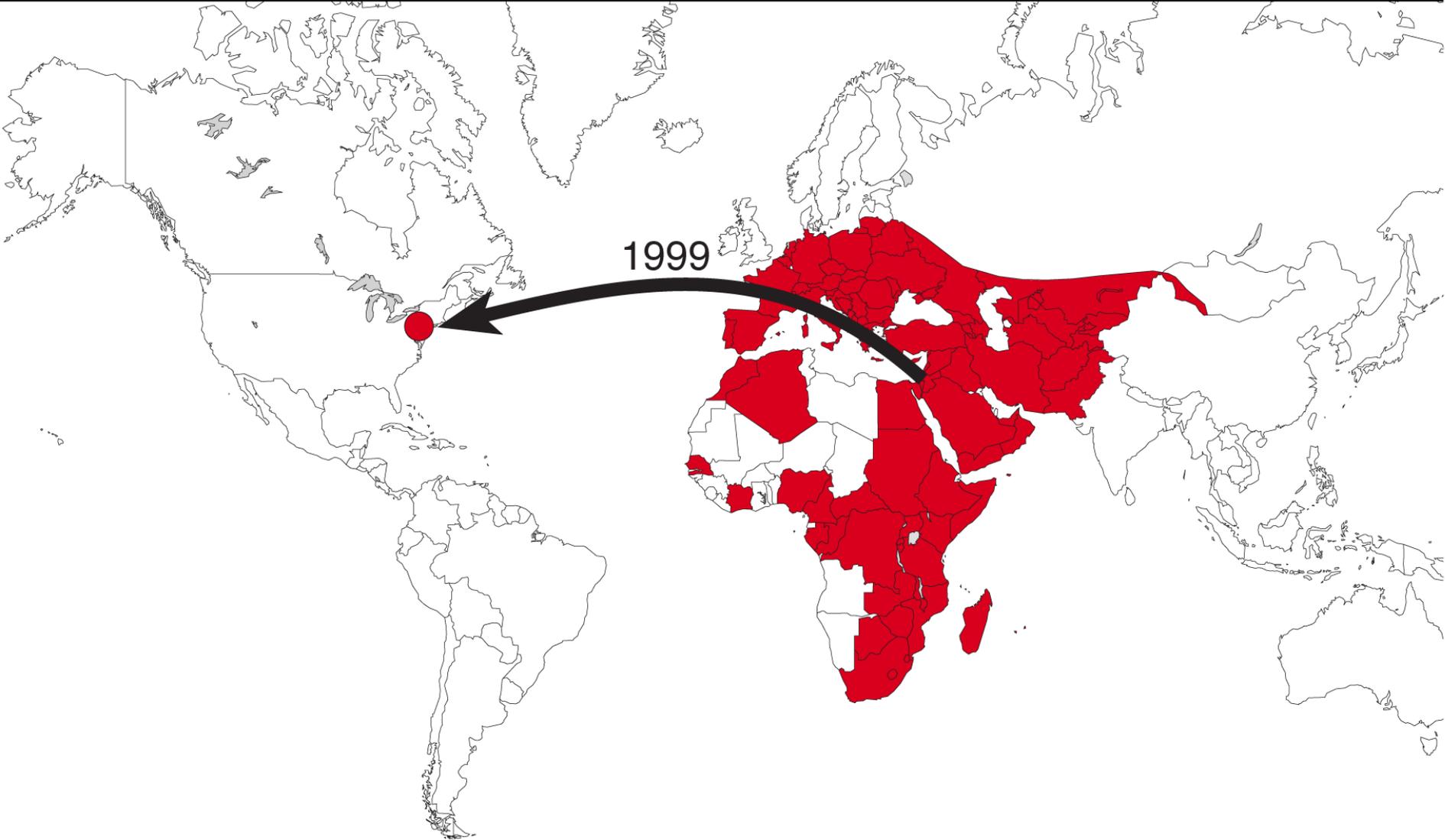
# Global Examples of Emerging and Re-Emerging Infectious Diseases

## West Nile virus



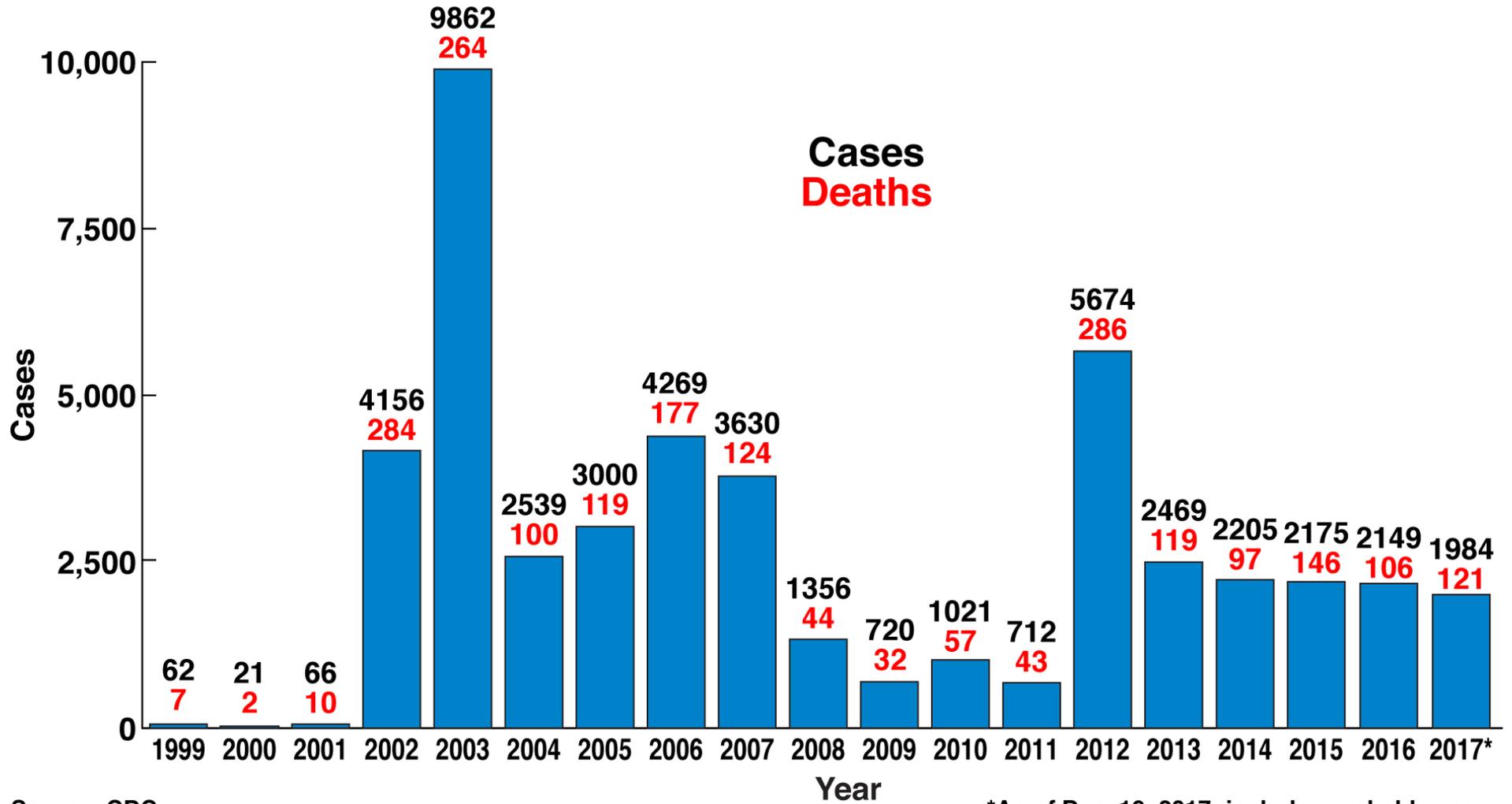
● Newly emerging    ● Re-emerging/resurging    ● “Deliberately emerging”

# Global Distribution of West Nile Virus, 1999



Source: CDC

# U.S. West Nile Virus Cases & Deaths, 1999-2017



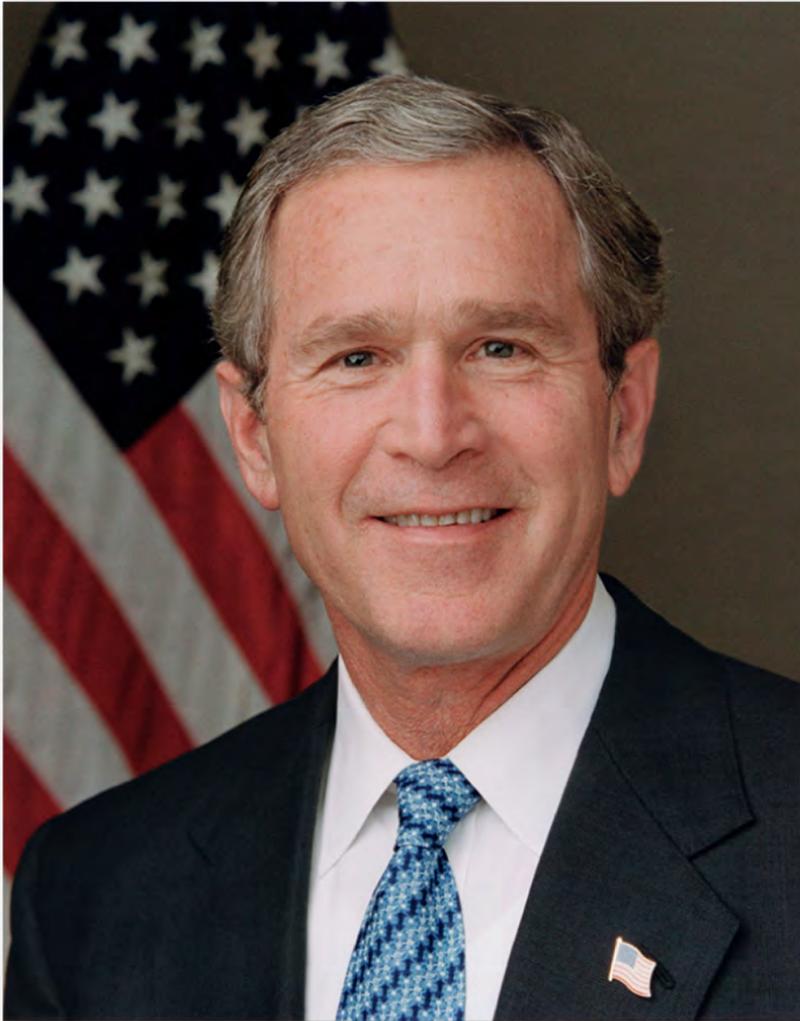
Source: CDC

Volume 203  
Issue 10  
May 15, 2011

# The Journal of Infectious Diseases

## **A West Nile Virus DNA Vaccine Utilizing a Modified Promoter Induces Neutralizing Antibody in Younger and Older Healthy Adults in a Phase I Clinical Trial**

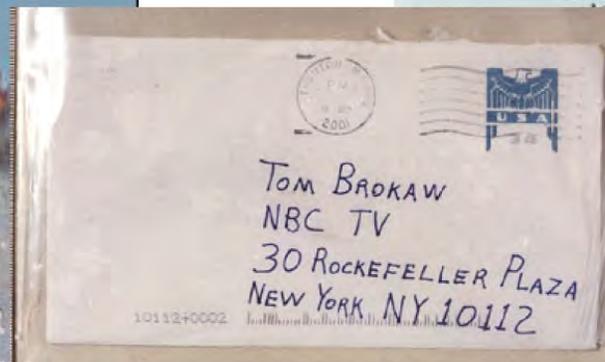
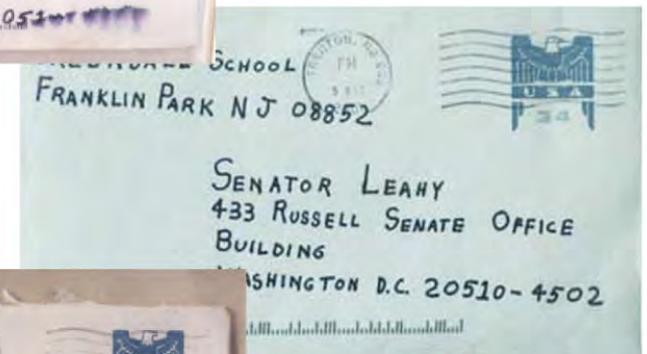
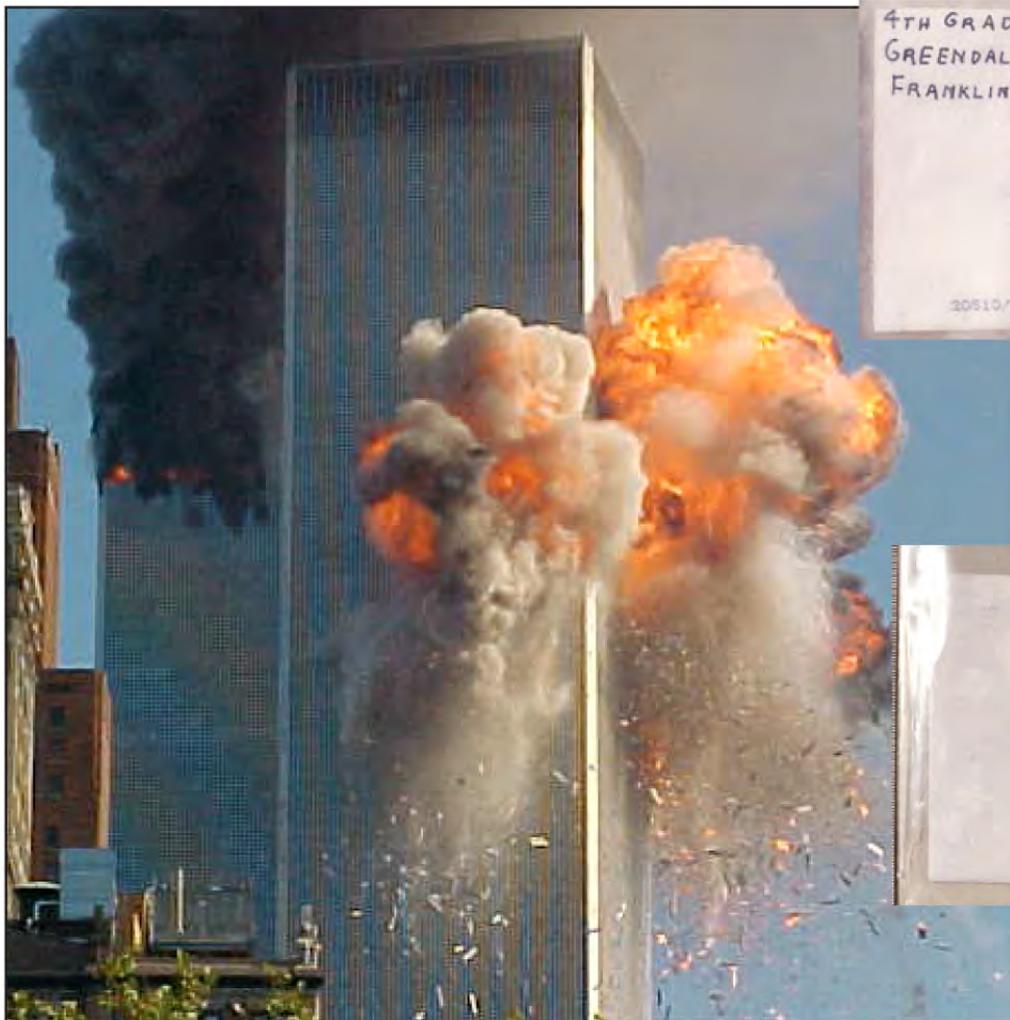
JE Ledgerwood, BS Graham et al. for the VRC 303 Study Team



**George W. Bush  
2001-2009**

- **HIV/AIDS**
- **Anthrax**
- **H5N1 Influenza**
- **SARS**

# Juxtaposition of Events of September 11, 2001 and the Deliberate Release of Anthrax





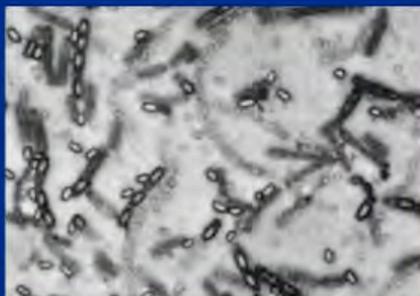
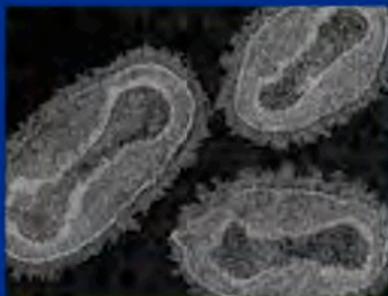
# **Bioterrorism: A Clear and Present Danger**

**HC Lane, J La Montagne and AS Fauci**



February 2002

## NIAID Strategic Plan for Biodefense Research



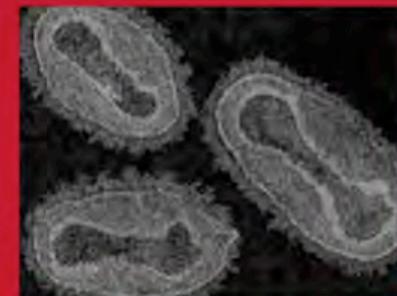
Responding  
Through  
Research



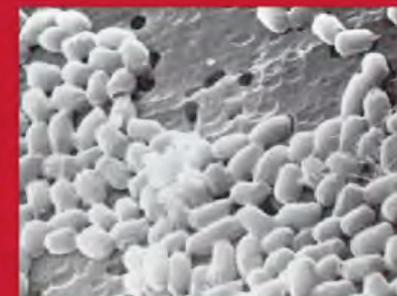
National Institute of Allergy and Infectious Diseases  
NATIONAL INSTITUTES OF HEALTH

February 2002

## NIAID Biodefense Research Agenda for CDC Category A Agents



Responding  
Through  
Research



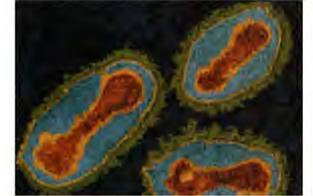
National Institute of Allergy and Infectious Diseases  
NATIONAL INSTITUTES OF HEALTH

# Category A Select Agents: Key Achievements

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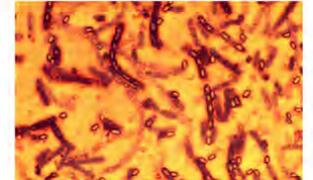
## ■ Smallpox

- Dryvax; MVA; antiviral drug



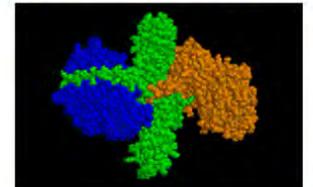
## ■ Anthrax

- Next-generation 2-dose vaccine; antitoxins



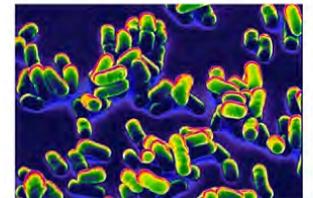
## ■ Botulinum

- Antitoxins; mAbs



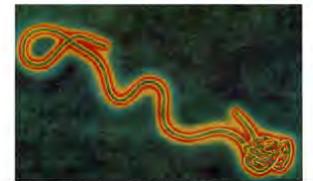
## ■ Plague

- Antibiotics



## ■ Ebola

- First human vaccine trials; therapeutics; diagnostics



# February 5, 2002

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**President GW Bush:** “Tony, what scares you the most among potential microbial threats that a terrorist might use?”

**Fauci:** “Mr. President, I worry more about the natural occurrence of an influenza pandemic and the ongoing plague of HIV than I do about a bioterror attack.”

# Newsday

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November 18, 2001

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## **The Worst Bioterrorist May Be Nature Itself**



The  
New England  
Journal of Medicine

Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

VOLUME 353

SEPTEMBER 29, 2005

NUMBER 13

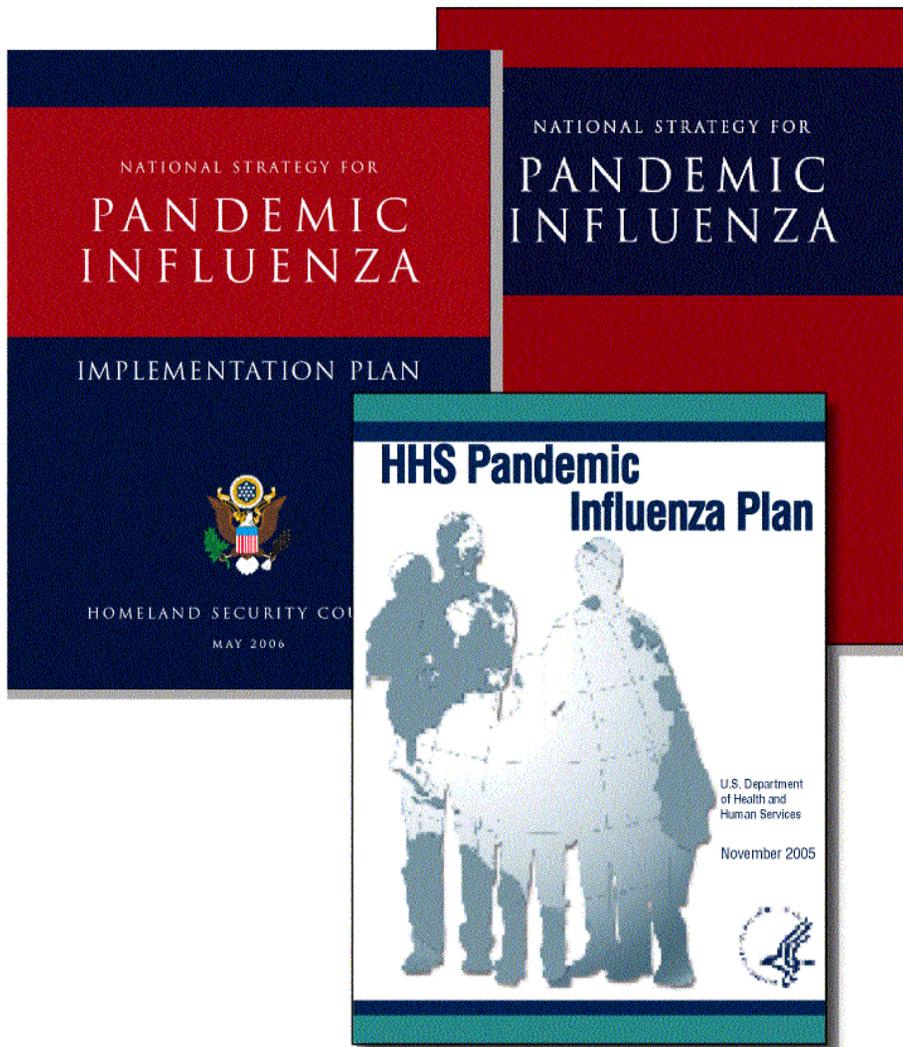
**REVIEW ARTICLE**

**Avian Influenza A (H5N1)  
Infection in Humans**

**The Writing Committee of the World Health Organization  
(WHO) Consultation on Human Influenza A/H5**

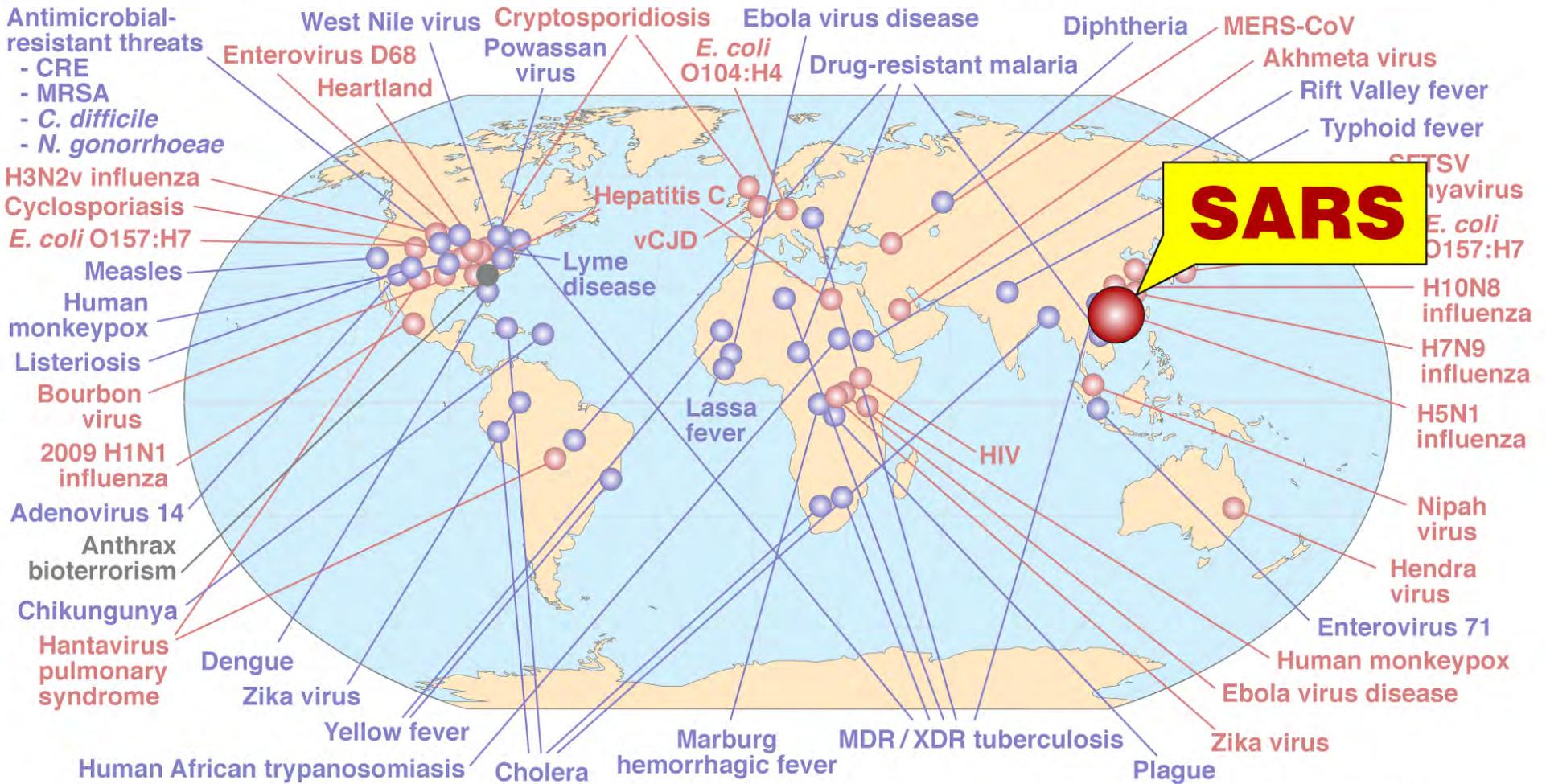
# Pandemic Influenza Preparedness Strategy and Implementation

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- **International Surveillance**
- **Domestic Surveillance**
- **Vaccines**
- **Antivirals**
- **Communications**
- **State and Local Preparedness**

# Global Examples of Emerging and Re-Emerging Infectious Diseases



● Newly emerging    
 ● Re-emerging/resurging    
 ● “Deliberately emerging”

# SARS: A New Challenge to Global Health

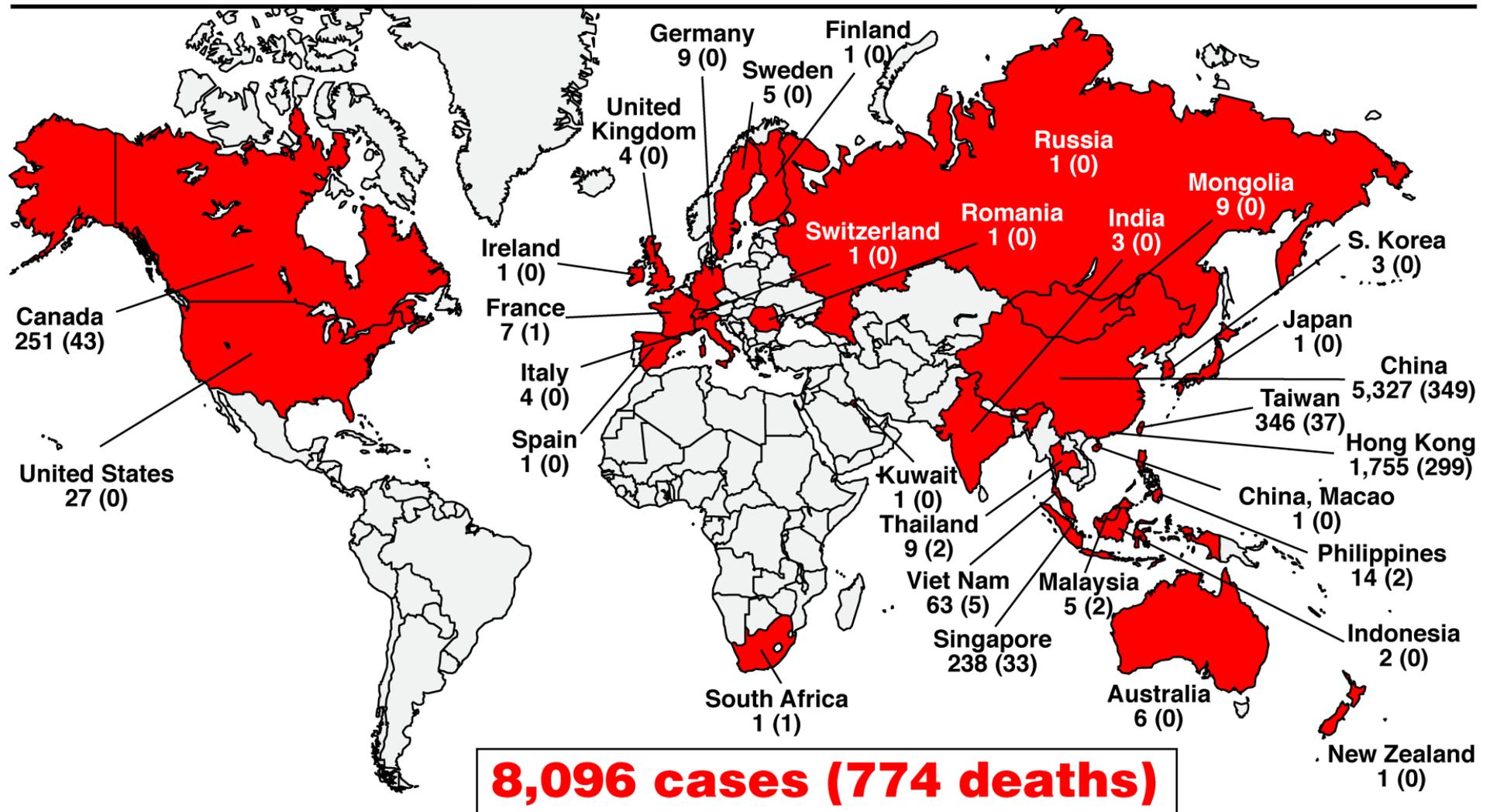


# Early Cases of SARS: Guangdong Province, China



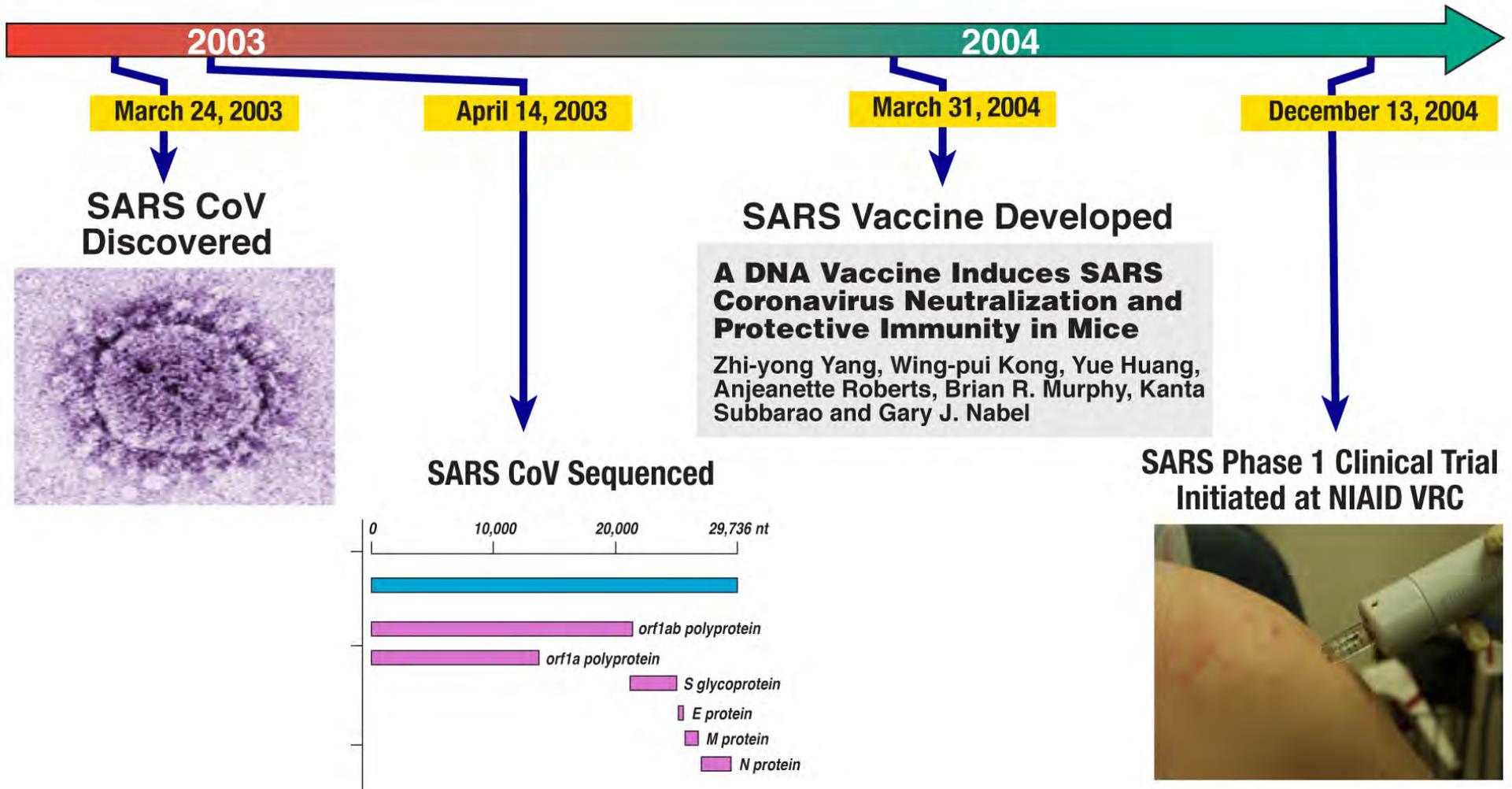


# Cumulative Reported Cases of SARS November 1, 2002 to July 31, 2003



Source: WHO

# SARS Characterization and Vaccine Development



**OTTAWA**



**CITIZEN**

July 6, 2003

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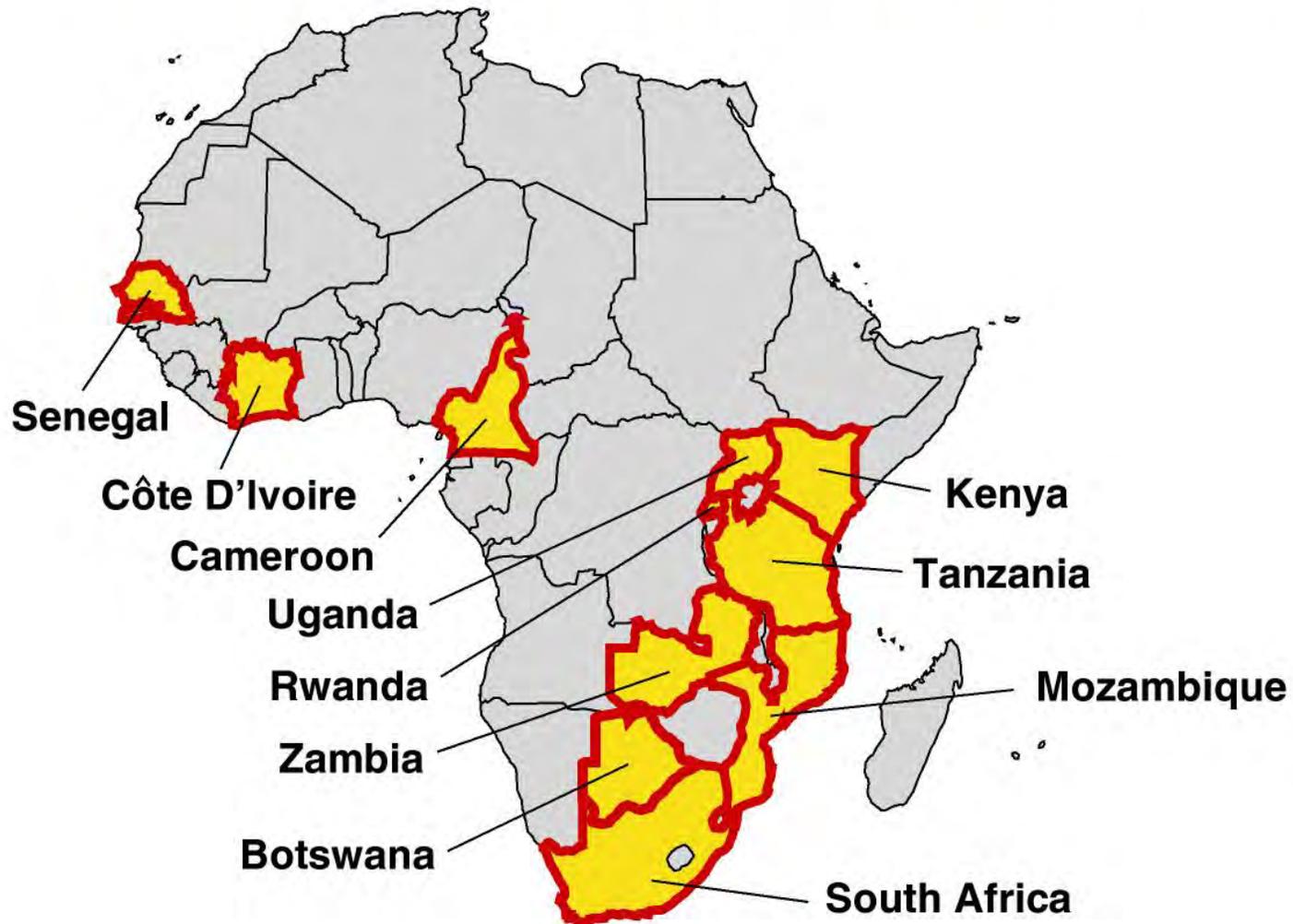
**WHO Declares Victory  
over SARS: Taiwan Last  
Country to Be Taken off  
List of Infected Areas**

# **The Birth of the President's Emergency Plan for AIDS Relief (PEPFAR)**



# Addressing HIV/AIDS: Visits to 11 Countries in Sub-Saharan Africa

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# The President's Emergency Plan for AIDS Relief – \$15B Over 5 Years

## Goals:

- Prevent 7 million new infections
- Treat 2 million HIV-infected people
- Care for 10 million HIV-infected people, orphans and other vulnerable children





## **State of the Union Address, January 28, 2003**

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- **President Bush announces the President's Emergency Plan for AIDS Relief (PEPFAR)**

# **Selected PEPFAR Accomplishments**

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**As of 9/30/2017:**

- **13.3 million people on antiretroviral therapy**
- **2.2 million perinatal HIV infections averted**
- **85.5 million people received HIV testing services in FY 2017**
- **25-40% decline in new HIV diagnoses among adolescent girls and young women through comprehensive HIV prevention interventions – DREAM partnership**

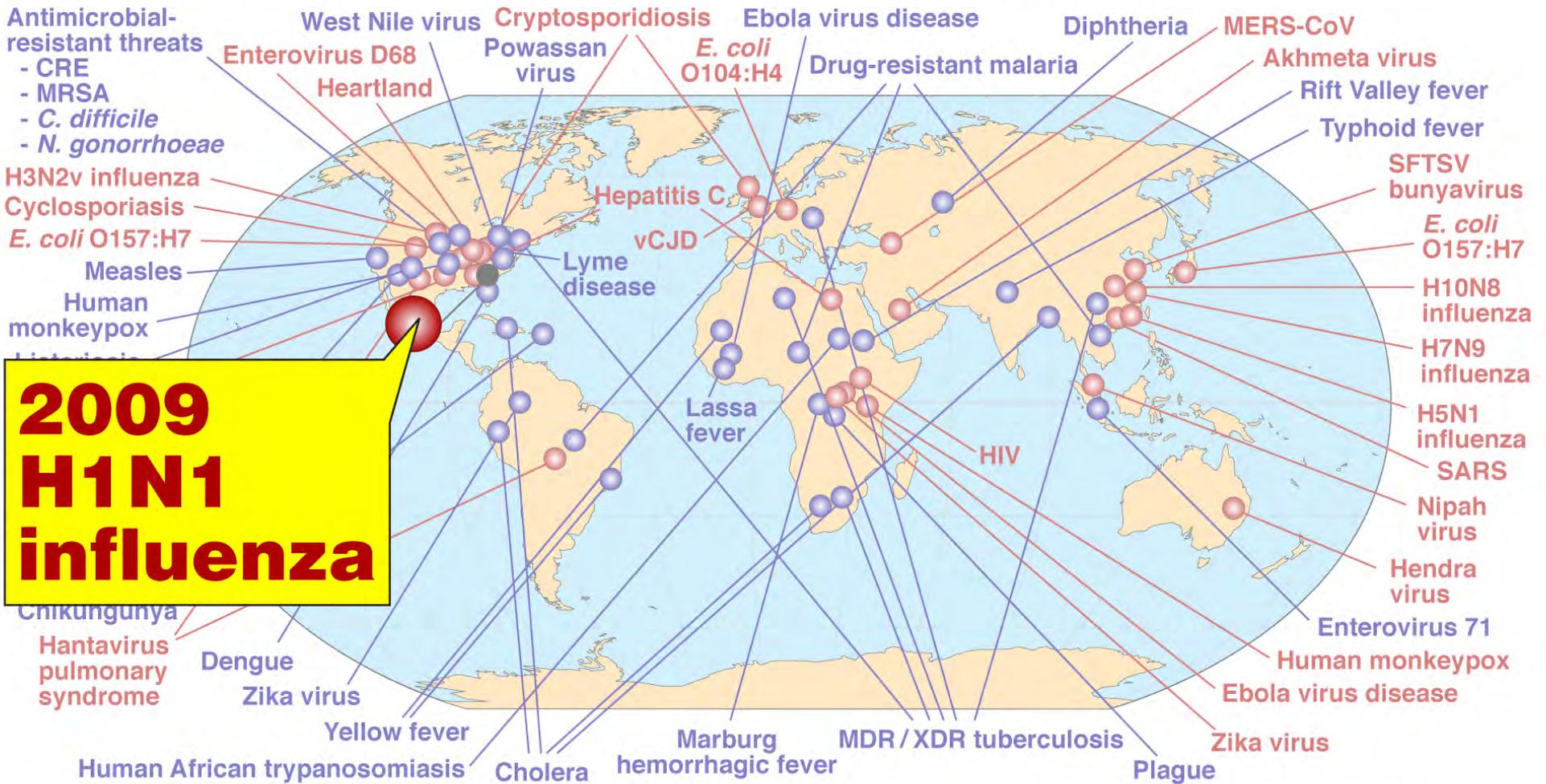




**Barack H. Obama  
2009-2017**

- **H1N1  
Pandemic  
Influenza**
- **MERS**
- **Chikungunya**
- **Ebola**
- **Zika**
- **Antimicrobial  
Resistance**

# Global Examples of Emerging and Re-Emerging Infectious Diseases



**2009  
H1N1  
influenza**

● Newly emerging    ● Re-emerging/resurging    ● "Deliberately emerging"



# Beginning of Global H1N1 Influenza as of March, 2009

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Source: WHO

# Global H1N1 Influenza Cases, as of April 29, 2009



Source: WHO

# Senate Appropriations Subcommittee Hearing on H1N1 Influenza, April 28, 2009

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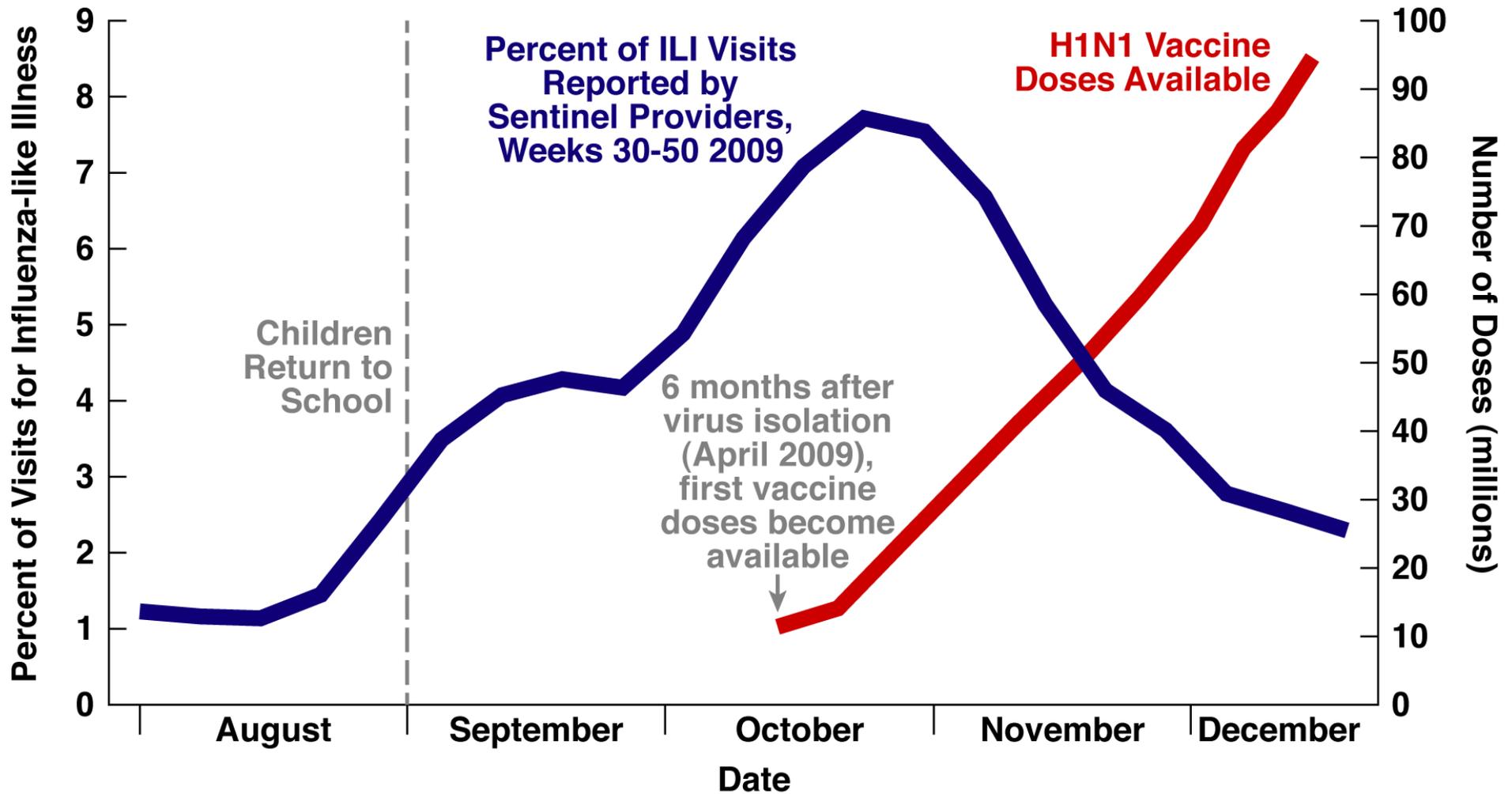
# Countries with Confirmed Pandemic (H1N1) 2009 Influenza Cases as of Sept. 30, 2009

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Source: WHO

# Vaccine Lags Behind 2009 H1N1 Influenza Pandemic

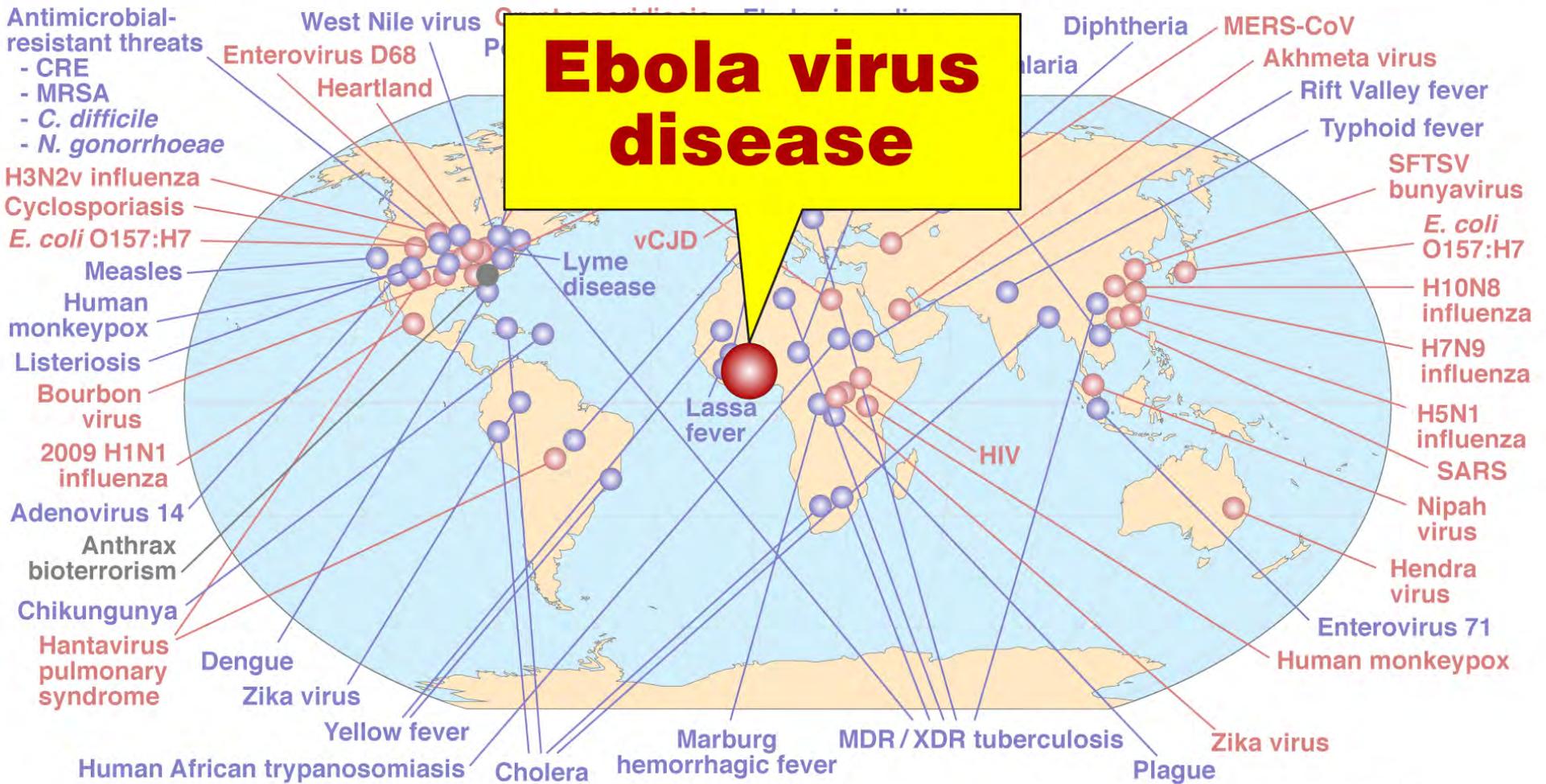


# House Oversight and Government Reform Committee Hearing on H1N1 Influenza Vaccines, Sept. 29, 2009

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# Global Examples of Emerging and Re-Emerging Infectious Diseases



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# Reported Ebola Virus Disease Cases in Guinea, Liberia, and Sierra Leone, 2014-2016

**Guinea**  
3,814 cases / 2,544 deaths



**Sierra Leone**  
14,124 cases / 3,956 deaths

**Liberia**  
10,678 cases / 4,810 deaths



**Total\*:**  
**28,616 cases**  
**11,310 deaths**

**40% mortality**

\*Confirmed, probable and suspected cases

Source: WHO, 12/2016



The  
New England  
Journal of Medicine

Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

Vol. 377

October 12, 2017

No. 15

# **Phase 2 Placebo-Controlled Trial of Two Vaccines to Prevent Ebola in Liberia**

SB Kennedy, HC Lane et al. for the PREVAIL I Study Group

- **Randomized, placebo-controlled Phase 2 trial of ChAd3-EBO-Z (GSK) and rVSVΔG-ZEBOV-GP (Merck)**
- **By 1 month, vaccines had elicited immune responses that were largely maintained through 12 months**
- **Trial rapidly initiated and completed; showed that rigorous research can be conducted during an outbreak**

# First Case Diagnosed in the U.S.: Timeline

**Sept 19**  
Subject  
departs  
Monrovia

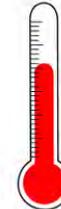


**Sept 20**  
Arrives  
and  
departs  
Brussels,  
Belgium

**Sept 20**  
Arrives in  
Dallas



**Sept 24**  
Develops  
symptoms



**Sept 26**  
Presents to ER,  
sent home



**Sept 28**  
Patient transferred by  
ambulance, admitted



**Sept 30**  
Tests positive for  
Ebola



**Oct 8**  
Patient **dies**

# **First Two Ebola Transmissions Within the U.S.**

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**The New York Times**

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October 12, 2014

**Texas Health Worker Tests Positive for Ebola**

**2nd Ebola Case in U.S. Stokes Fears of Health Care Workers**



# **NIH Special Clinical Studies Unit: Designated Ebola Treatment Facility**

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\*As of Oct. 2014, three Designated Ebola Treatment Facilities existed in the U.S.

# The Washington Post

October 25, 2014

## **Nina Pham, Nurse Who Contracted Ebola, is Now Free of Virus and Leaves NIH**



Photo: The Washington Post



Photo: Nina Pham



March 12, 2015

# **U.S. Ebola Patient Headed to NIH**













National Institutes of Health  
*Turning Discovery Into Health*



U.S. Department of Health and Human Services

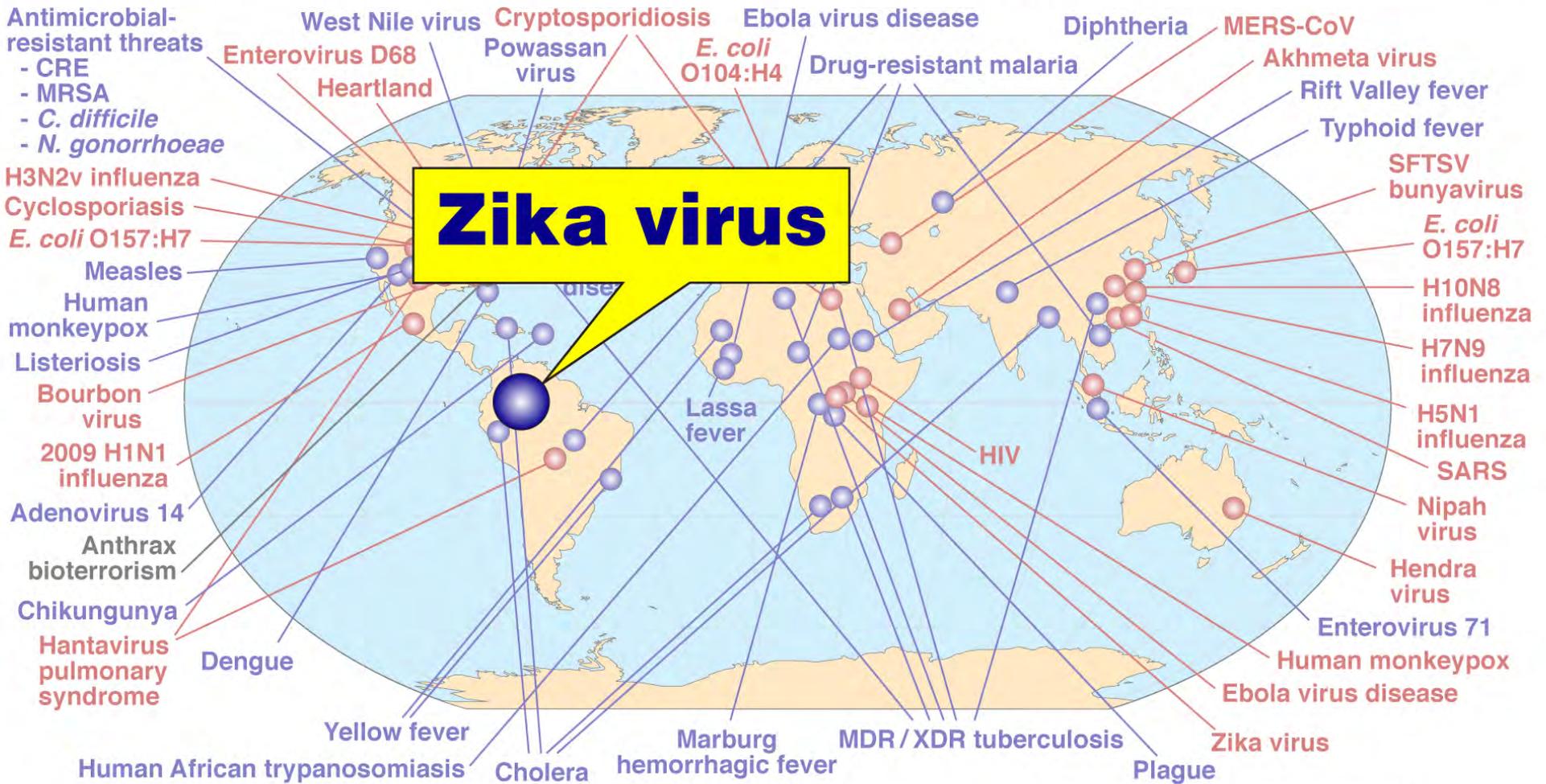
**NIH News**

National Institutes of Health

Thursday, April 9, 2015

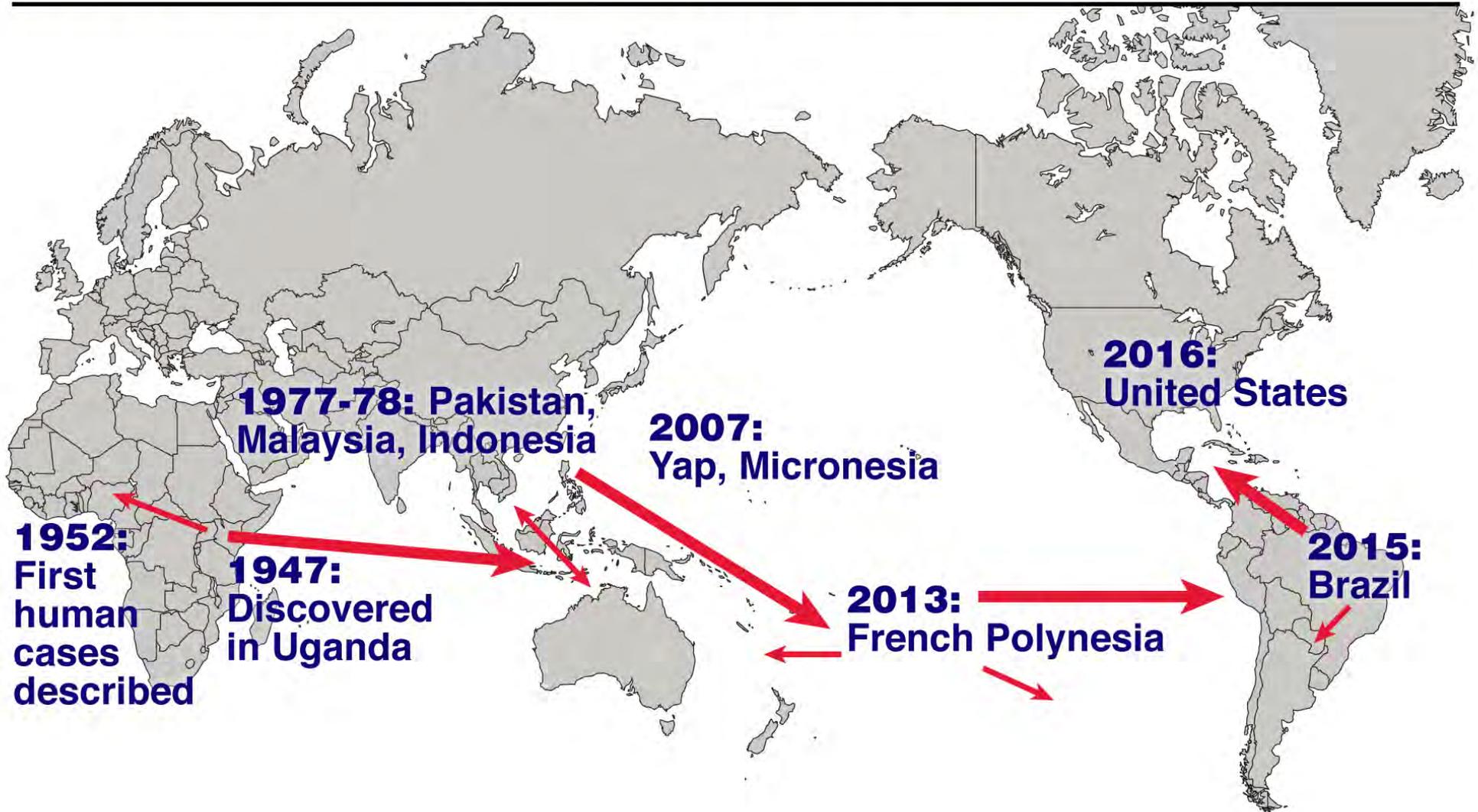
# **Patient Admitted With Ebola Virus Disease Discharged From NIH Clinical Center**

# Global Examples of Emerging and Re-Emerging Infectious Diseases



● Newly emerging    ● Re-emerging/resurging    ● “Deliberately emerging”

# Zika Virus Spread, 1947-2017



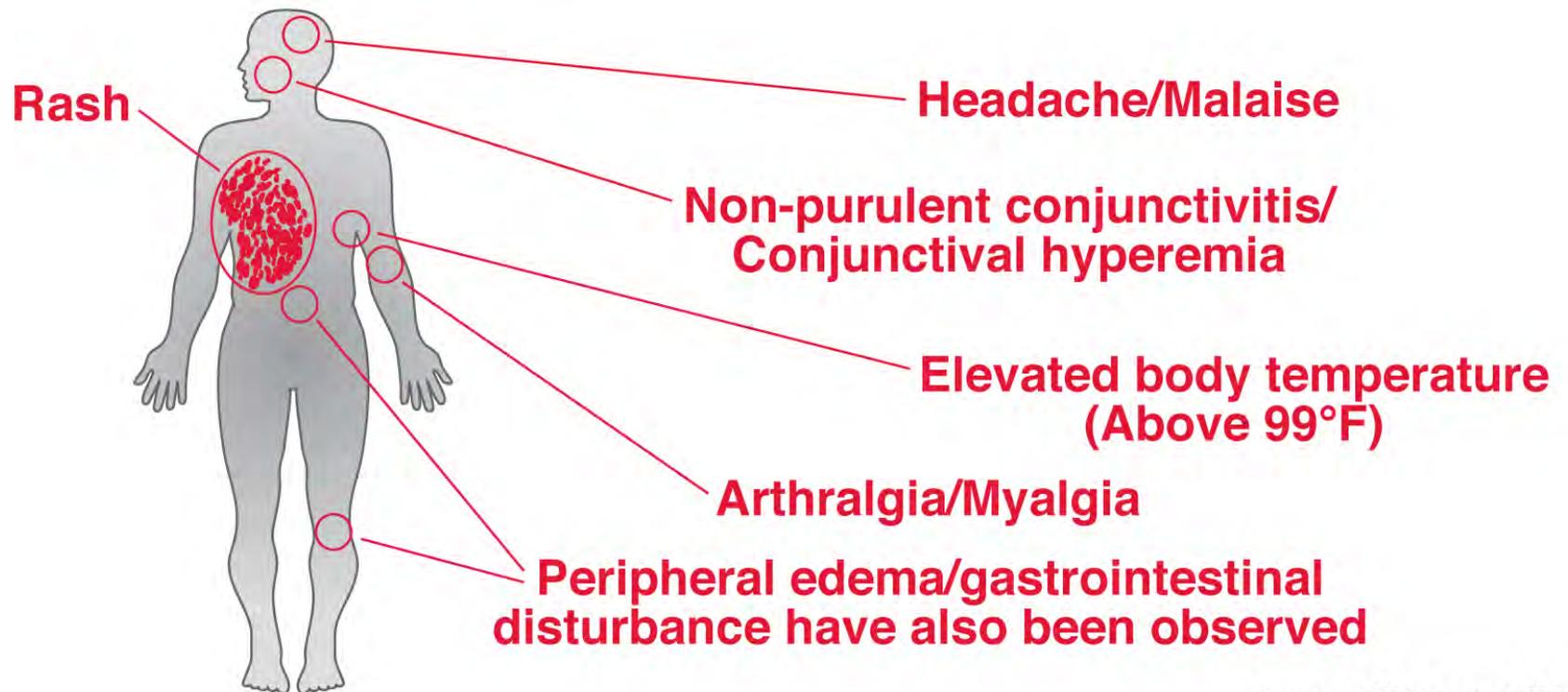
Source: Lancaster University

# Symptoms of Zika Virus Infection

■ 4 in 5 individuals *asymptomatic*

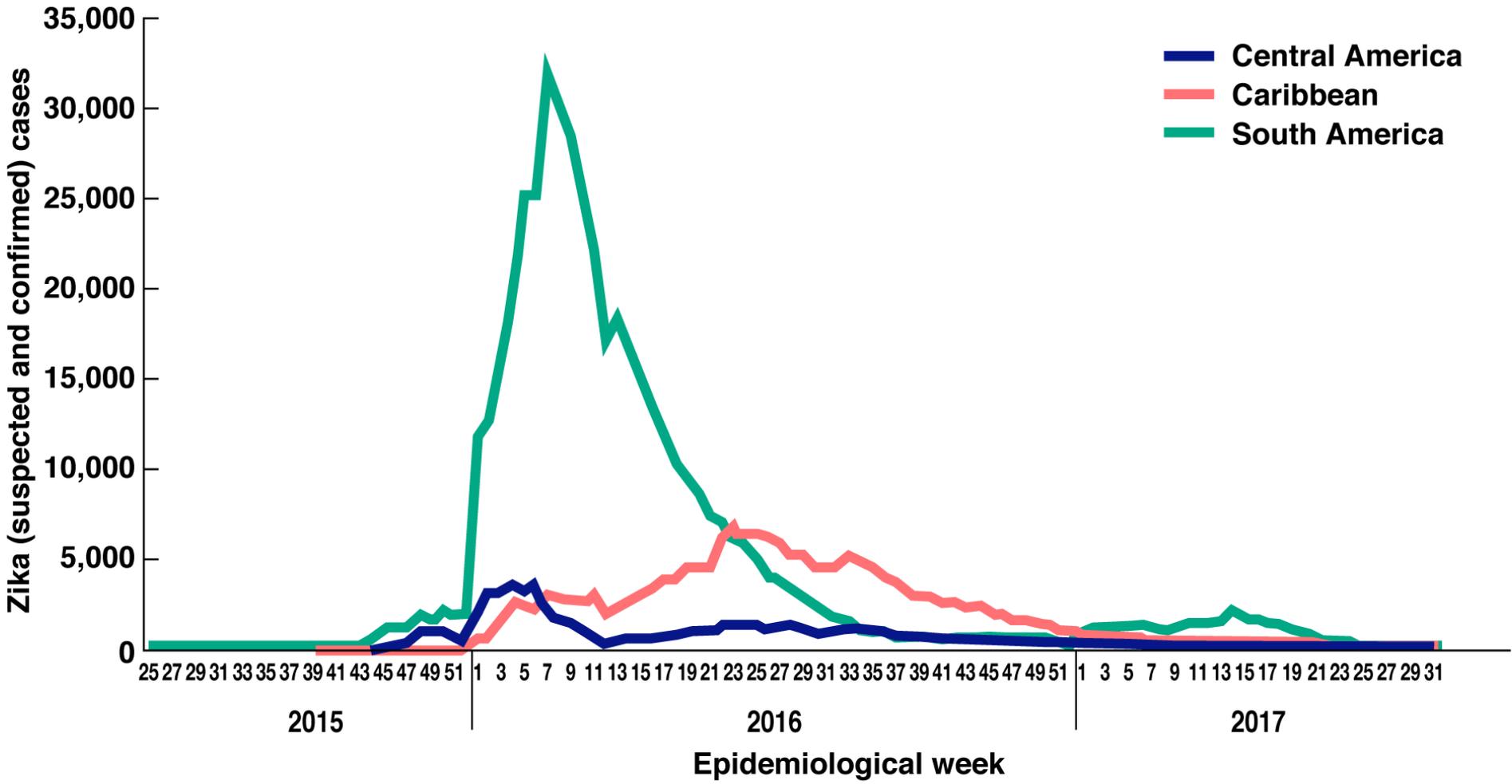
Incubation  
3-12 days

Mild symptoms  
2-7 days



Source: BMJ.com, 2/2016

# Suspected and Confirmed Zika Cases in the Americas, 2015-2017



Source: PAHO, 8/25/2017.

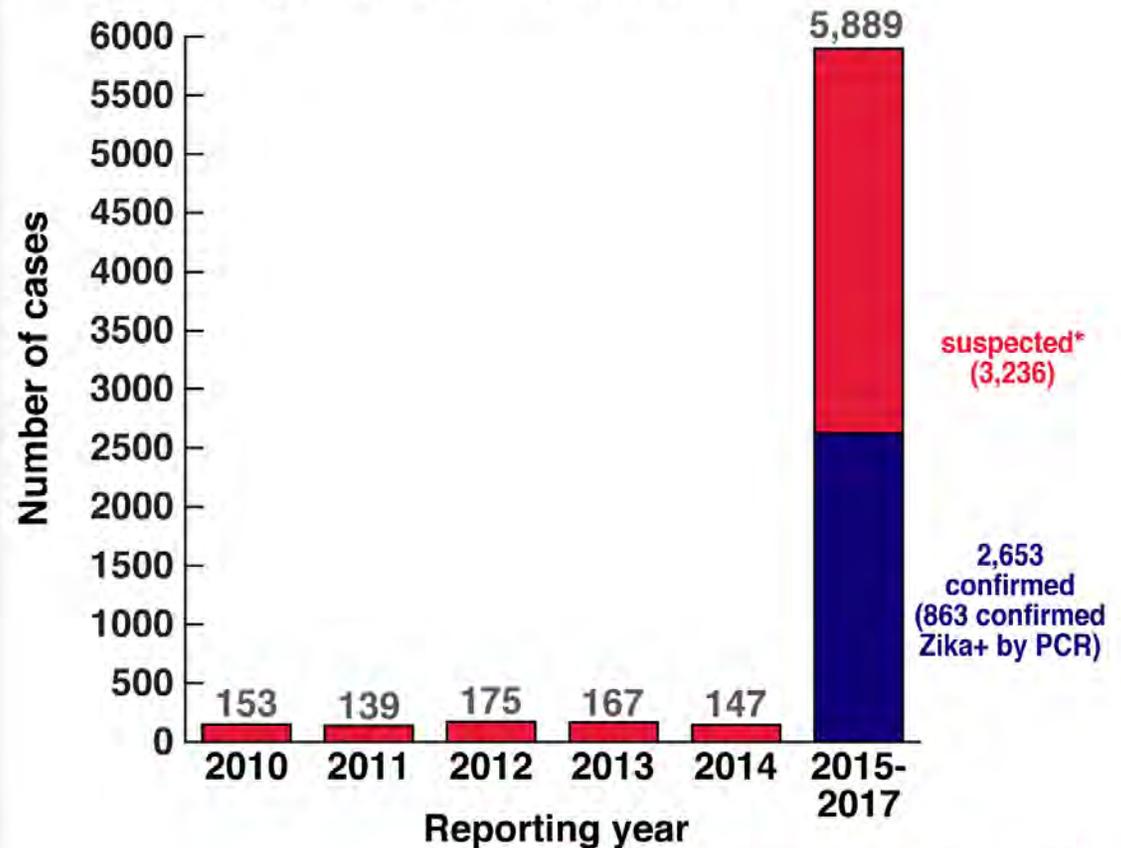
# Marked Increase in Microcephaly Cases in Brazil

Associated Press

November 30, 2015

## Brazil Links Mosquito-Borne Zika Virus to Microcephaly Birth Defect

Microcephaly cases in Brazil 2010-14; suspected/confirmed cases 2015-2017



\*does not include cases investigated and discarded

Source: Brazilian MOH; data as of April 26, 2017

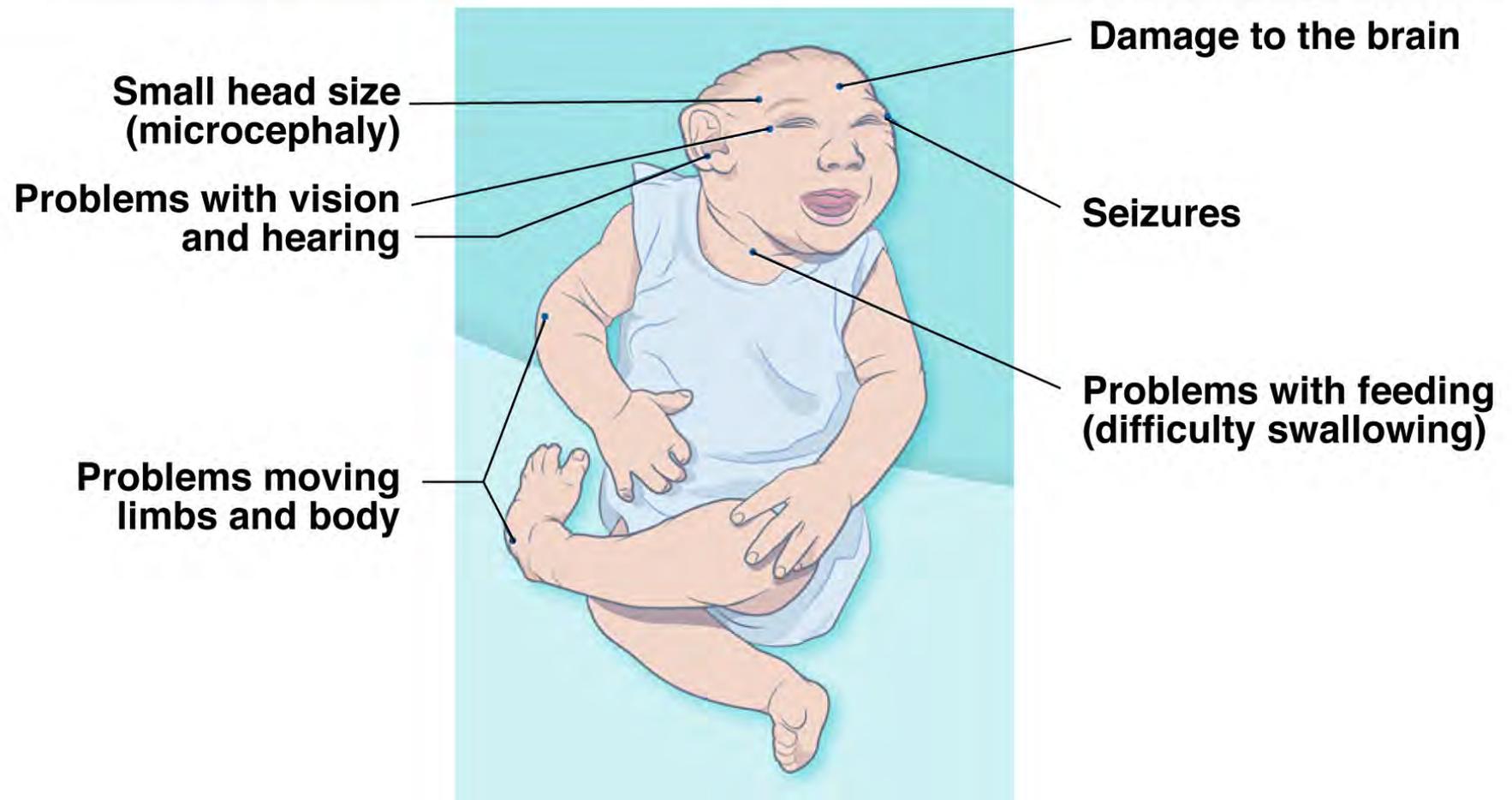
# **Baby Born With Microcephaly**

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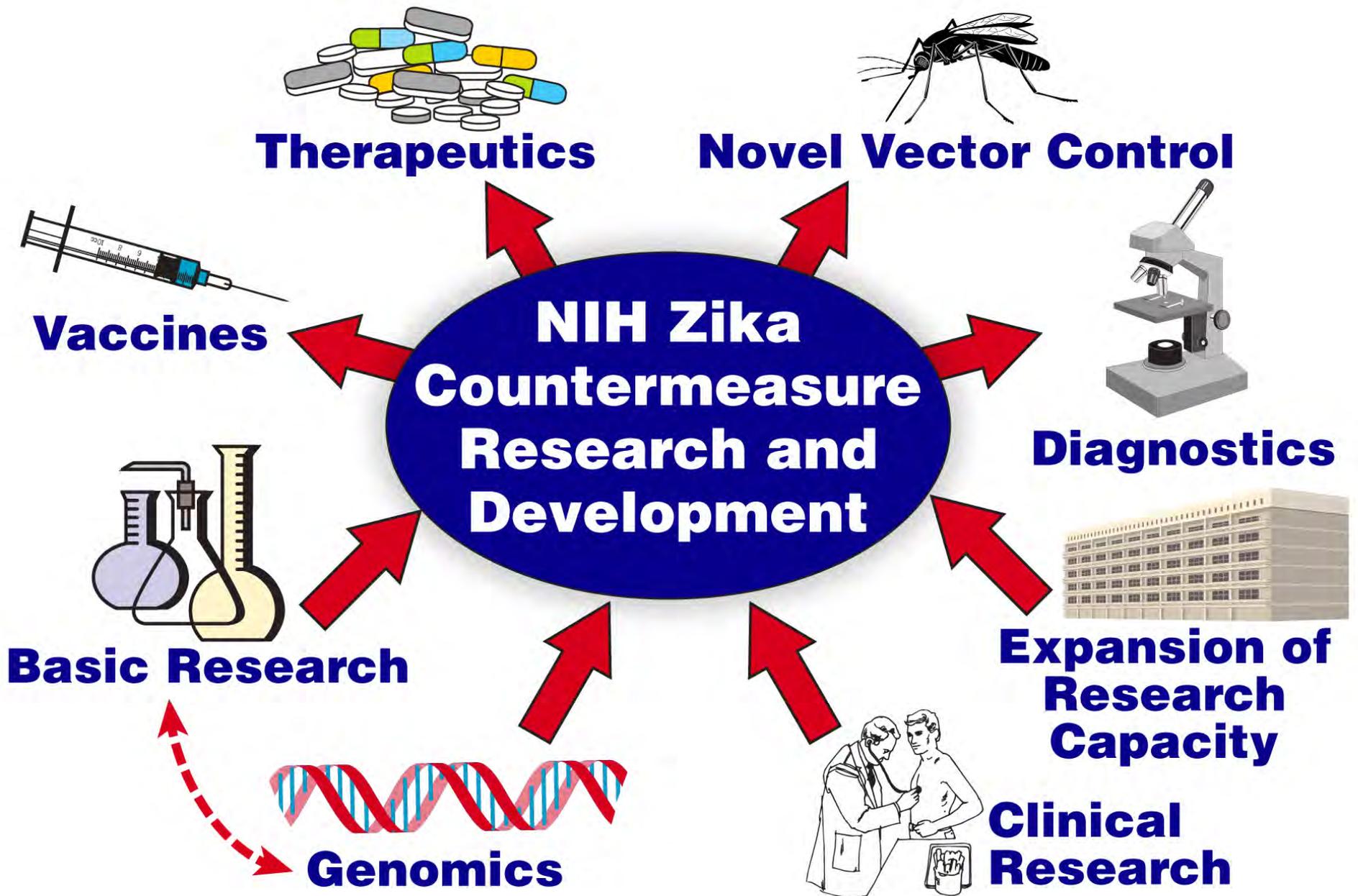


# **Congenital Zika Syndrome is a Pattern of Birth Defects in Babies Infected with Zika During Pregnancy**

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Source: CDC





**Therapeutics**



**Novel Vector Control**



**Vaccines**

**NIH Zika  
Countermeasure  
Research and  
Development**



**Diagnostics**



**Basic Research**



**Expansion of  
Research  
Capacity**



**Genomics**



**Clinical  
Research**

# **NIH Zika Vaccine Candidates**

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- **DNA vaccine (NIAID VRC)**
- **Zika purified inactivated vaccine (WRAIR/NIAID/BARDA and Sanofi Pasteur)**
- **Live-attenuated Zika/dengue chimeric virus (NIAID intramural/Butantan)**
- **mRNA vaccine candidate (NIAID VRC, GSK)**
- **Vesicular Stomatitis Virus vectored vaccine (NIAID extramural)**

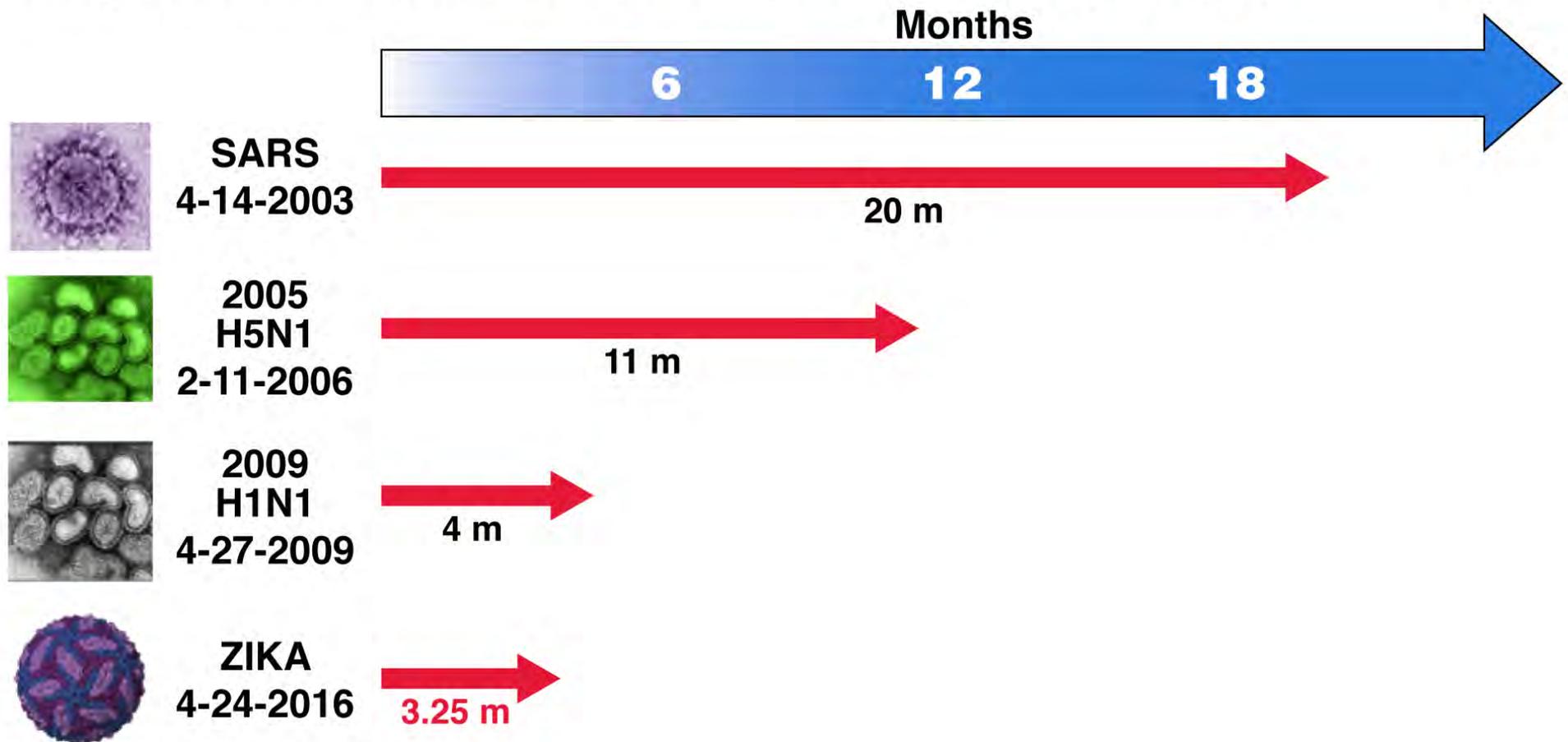
# **NIH Zika Vaccine Candidates**

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# VRC DNA Vaccines for Emerging Infections

## Sequence Selection to 1st Human Injection



Courtesy: J Ledgerwood/NIAID VRC

# Phase 2/2b Clinical Trial of VRC Zika DNA Vaccine

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## ■ Part A (non-placebo controlled)

- Launched 3/31/2017
- Fully enrolled – n=90

## ■ Part B (placebo-controlled)

- Launched 7/19/2017
- Target n=2,400 to 5,000



# Five Administrations and Emerging Infectious Diseases

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**Ronald W. Reagan 1981-1989**



**George H.W. Bush 1989-1993**



**William J. Clinton 1993-2001**



**George W. Bush 2001-2009**



**Barack H. Obama 2009-2017**



# **Six Administrations and Emerging Infectious Diseases**

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**Ronald W. Reagan 1981-1989**



**George H.W. Bush 1989-1993**



**William J. Clinton 1993-2001**



**George W. Bush 2001-2009**



**Barack H. Obama 2009-2017**



**Donald J. Trump 2017-present**



**What's Next?**

**THE  
HILL**

April 2, 2017

# **Health Officials Brace for Return of Zika**





Available online July 7, 2017

The Brazilian Journal of



**INFECTIOUS DISEASES**

**Will Mayaro Virus Be Responsible for the Next Outbreak of an Arthropod-borne Virus in Brazil?**

DLO Esposito, BAL daFonseca

**ScienceDaily**<sup>®</sup>

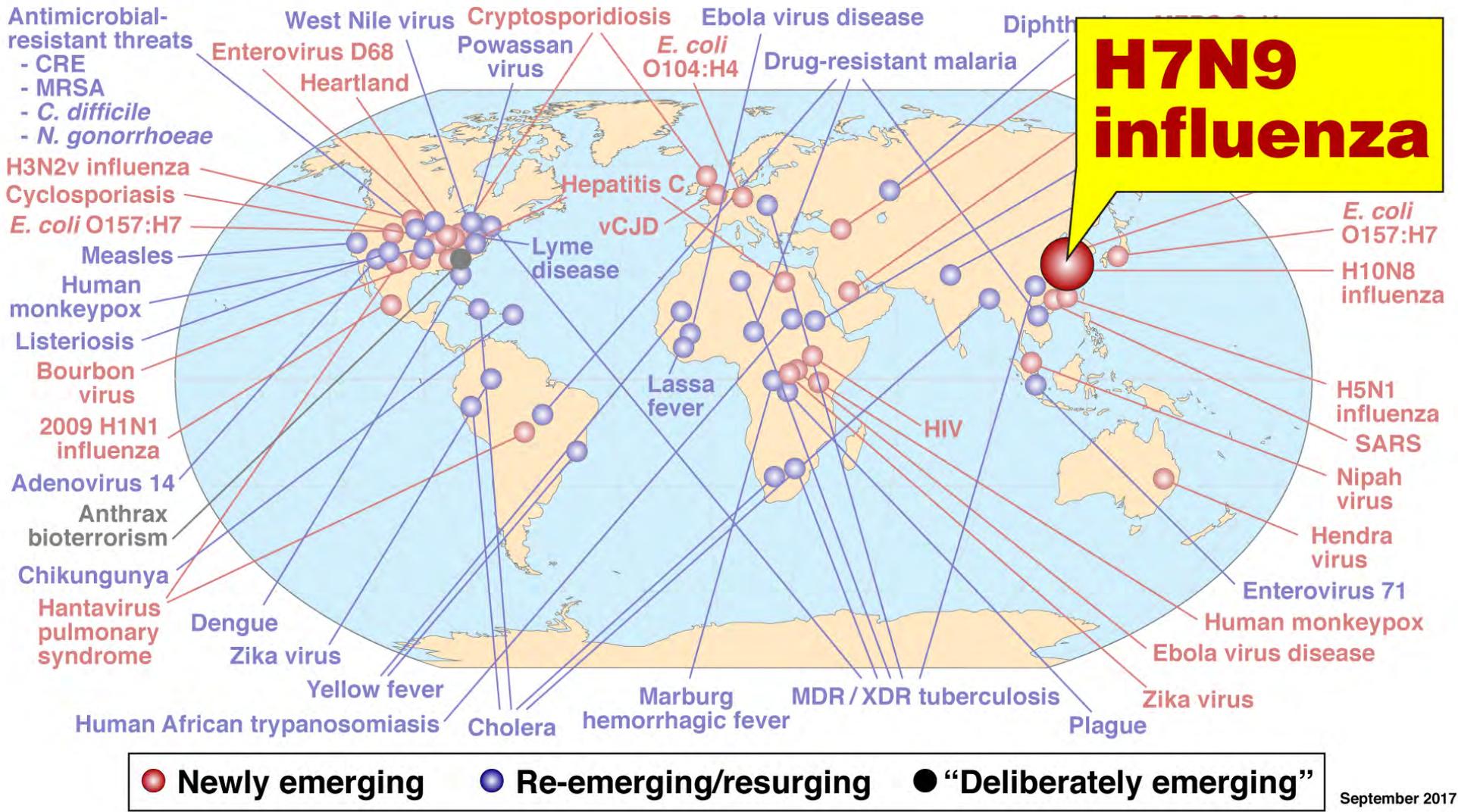
Your source for the latest research news

August 22, 2017

**Oropouche Virus Could Emerge and Cause a Public Health Problem**

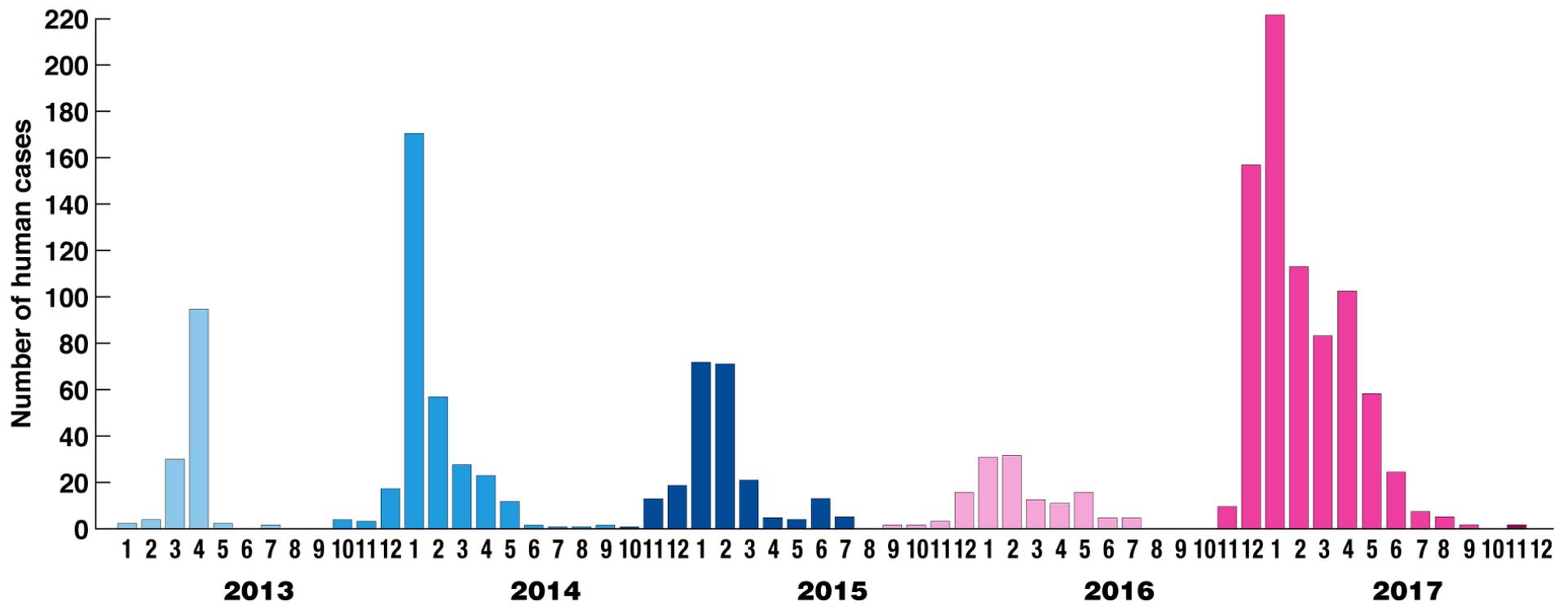
Vector is no longer confined to villages in the Amazon but is spreading to major cities throughout Brazil, researcher warns

# Examples of Recently Emergent Influenza Viruses

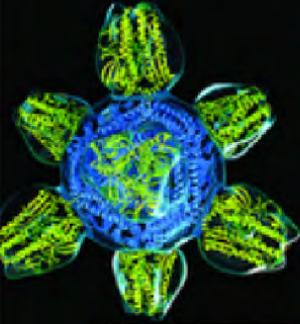


# Waves of Human H7N9 Influenza Infections in China, February 2013-present

- **1,623 confirmed human cases, 620 deaths**
- **5th wave: >50% of cumulative cases**



Source: FAO, 12/19/17



NIAID-Sponsored Workshop

# Pathway to a Universal Influenza Vaccine

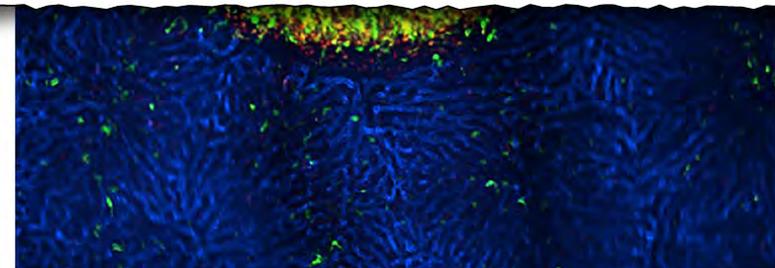
June 28-29, 2017

5601 Fishers Lane Conference Center  
Rockville, MD, USA

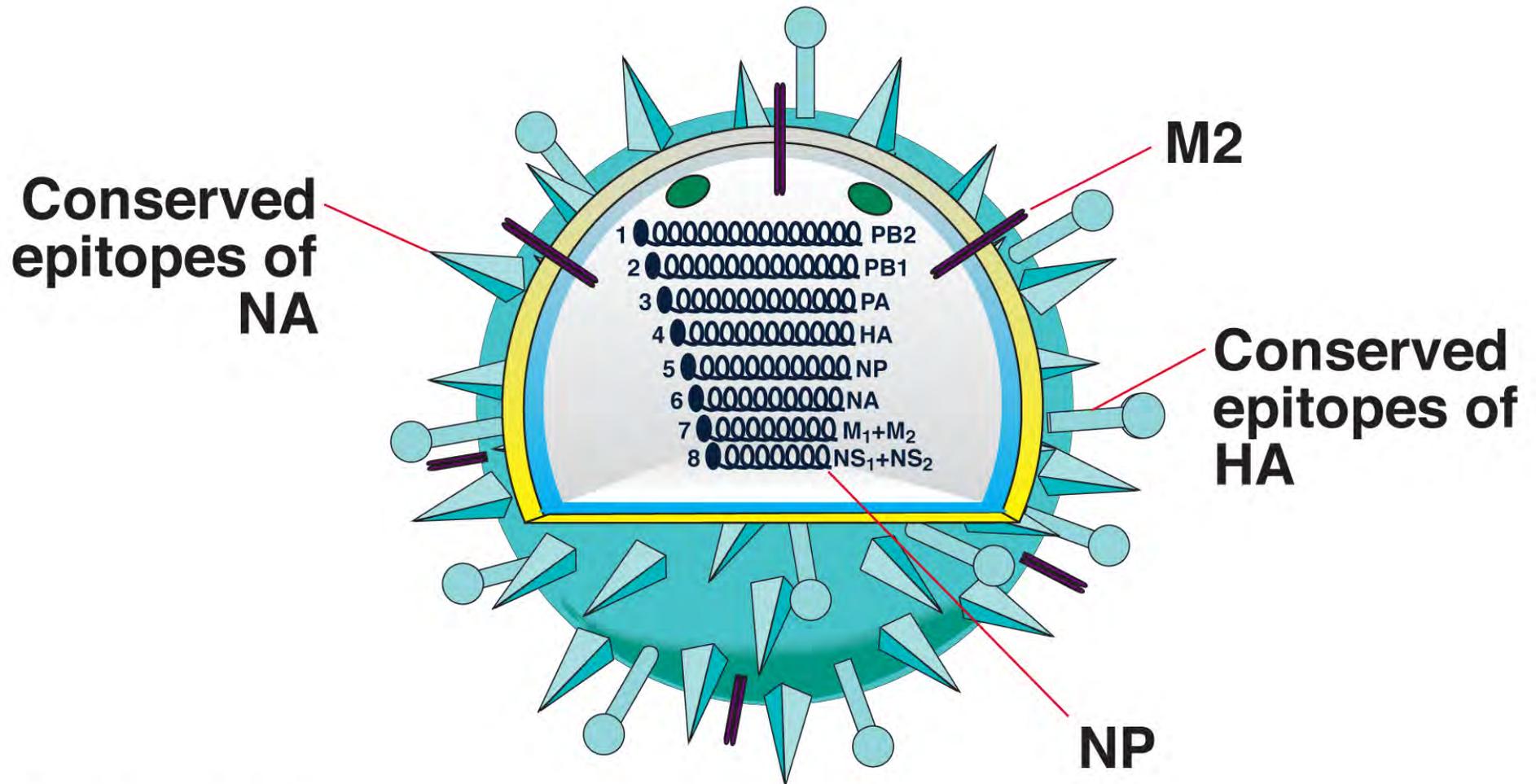


# The Pathway to a Universal Influenza Vaccine

CI Paules, HD Marston, RW Eisinger, D Baltimore, AS Fauci

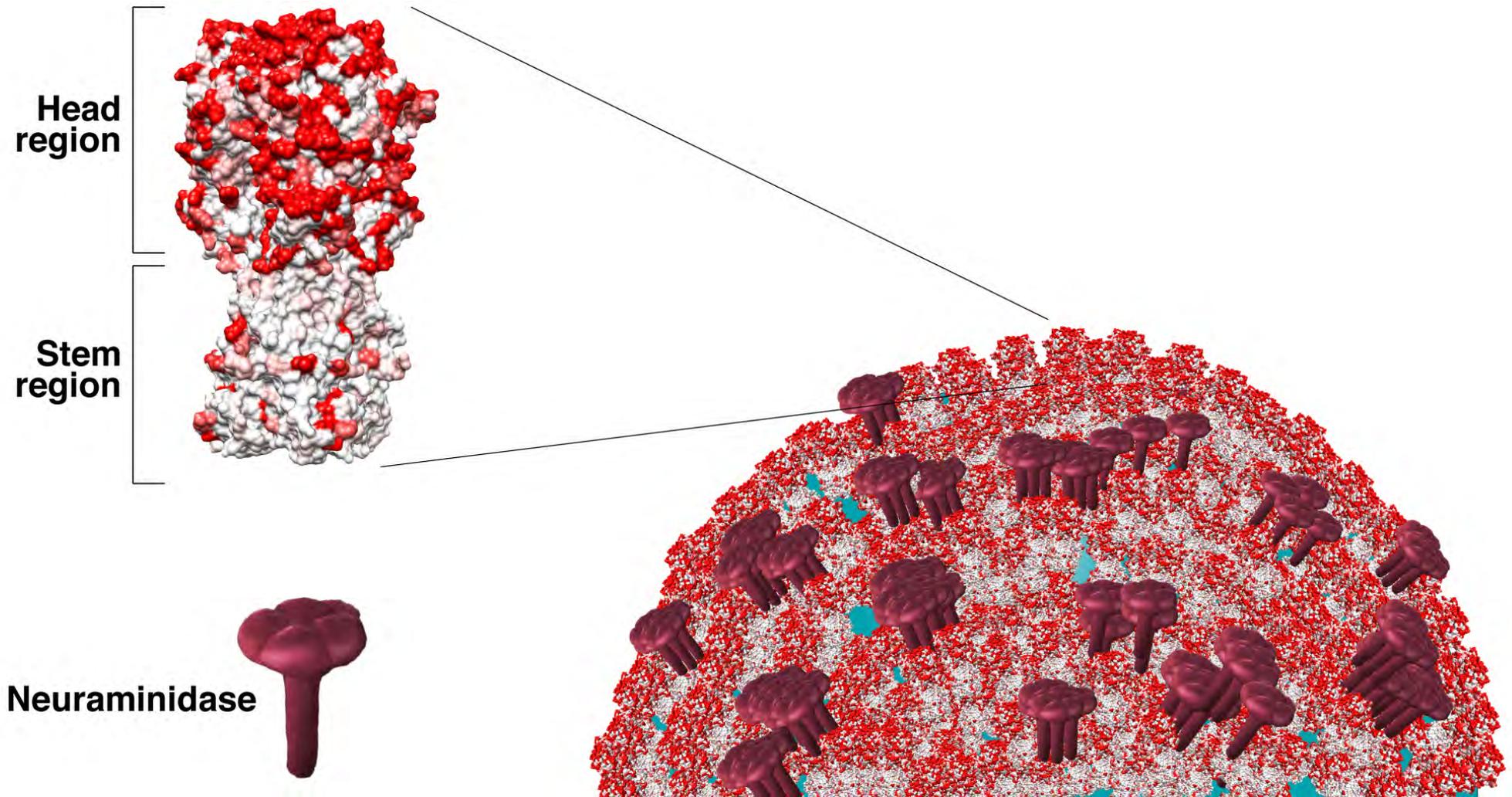


# Selected Targets for “Universal” Influenza Vaccines

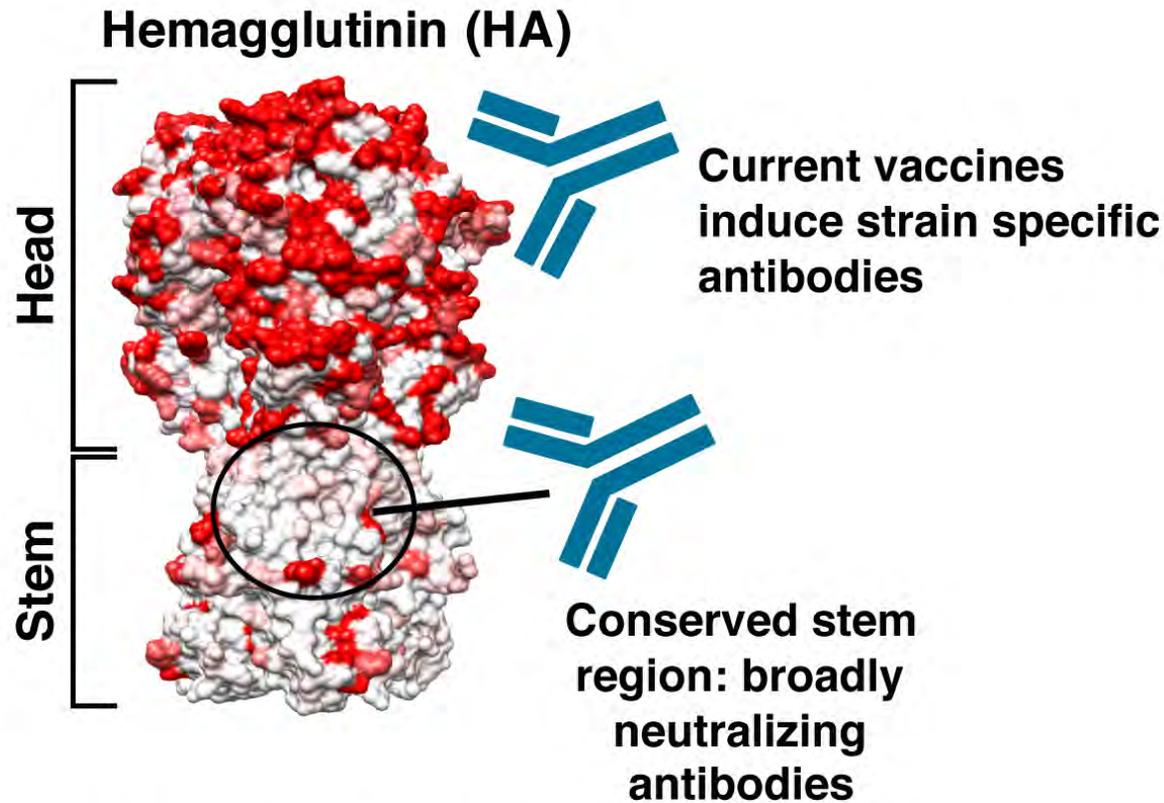


# Influenza A Hemagglutinin (HA)

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# Generating Broadly Neutralizing Antibodies: Targeting the Stem



H1N1 Sequence conservation



Courtesy Jeffrey Boyington

- Most antibodies bind to epitopes of highly variable head region
- Antibodies that neutralize multiple strains bind to a highly conserved area in the stem region

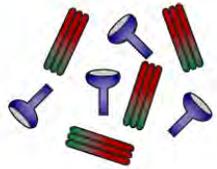
# **Evolution of Technologies for Influenza Vaccines**

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# New Platforms for Seasonal and Pandemic Influenza Vaccines

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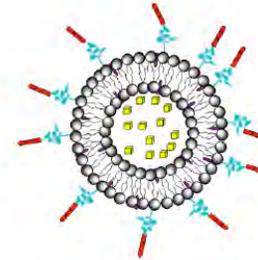
**Recombinant subunit**



**Synthetic peptide**



**Microbial vector**



**Nanoparticle-based**



**Virus-like particles  
(VLPs)**



**DNA-based**

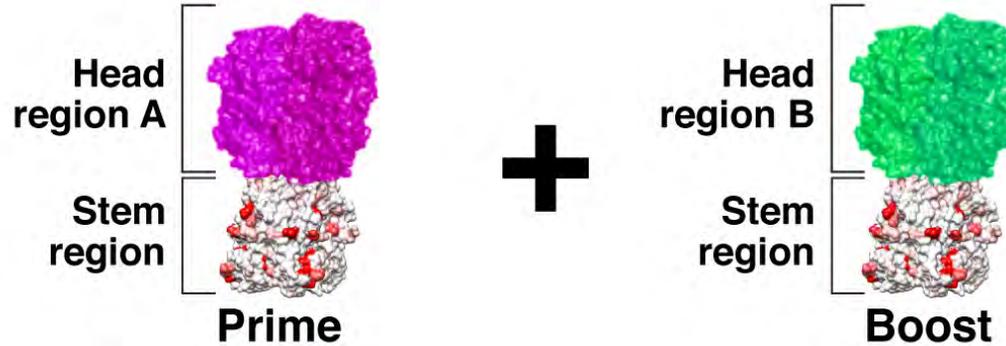


**Novel delivery systems  
(e.g., microneedles)**

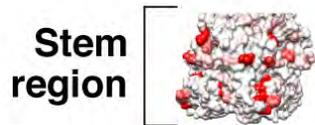
# Selected Approaches to Universal Influenza Vaccines

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**Chimeric HA**



**Stem only**



**Nanoparticle**



**Virus-like particle**



# Health Affairs **Blog**

February 9, 2017

## **What Three Decades Of Pandemic Threats Can Teach Us About The Future**

Anthony S. Fauci



***“If history has taught us anything, it is that the new administration is likely to experience at least one infectious disease crisis of significance.”***

# **Lessons Learned from Previous Pandemics**

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- **Global surveillance**
- **Transparency and communication**
- **Infrastructure and capacity building**
- **Coordinated and collaborative basic and clinical research**
- **Adaptable platform technologies for vaccines, diagnostics and therapeutics**
- **Stable funding mechanism – “Public Health Emergency Fund”**

Volume 8, Issue 11

November 2008

THE LANCET Infectious Diseases



# **Emerging Infections: A Perpetual Challenge**

**DM Morens, GK Folkers & AS Fauci**

